



DIAGNOSE & TREAT WITH EXPERTISE

DOCTOR ON DUTY

TREATMENT GUIDE

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A comprehensive, step-by-step guide to assist you in clinical practice, covering the most common diseases. Designed for House officers, Medical officers, General practitioners, interns, and trainees.



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TABLE OF CONTENTS

CHAPTERS/TOPICS	PAGE NO.
CHAPTER-1 HISTORY & PHYSICAL EXAMINATION	01
CHAPTER-2 SYMPTOMS & QUESTIONARY	13
CHAPTER-3 PROCEDURES & WARD SKILLS	
1. Passing IV line (IV cannulation)	17
2. Setting up an infusion set (a drip set)	18
3. Venepuncture (phlebotomy)	19
4. Vacutainer tube guide (collection containers)	21
5. Blood tube (Vacutainer) color chart	22
6. Blood cultures	23
7. Blood transfusion	24
8. Guidelines for blood transfusion	25
9. Arterial blood gases (ABGs) sampling	27
10. Arterial blood gases (ABGs) interpretation	28
11. Injection method (intramuscular, subcutaneous & intradermal)	29
12. Nasogastric (NG) intubation	31
13. Urinary catheterization	32
14. Endotracheal intubation	34
15. Sterile suctioning procedure	36
16. Knee arthrocentesis (knee joint aspiration)	37
17. Lumbar puncture (spinal tap)	38
18. Ascitic tap (Diagnostic paracentesis, Paracentesis abdominis)	40
19. Pleural tap (thoracentesis/thoracocentesis)	42
20. Bedside blood glucose measurement	44
CHAPTER-4 PRESCRIBING, ADMINISTRATIVE & COMMUNICATION SKILLS	
1. Explaining clinical skills	45
2. Patient counselling for endoscopic procedure	46
3. Upper endoscopy counselling	46
4. Lower endoscopy counselling	47
5. Obtaining medical consent	48
6. Breaking bad news & Discussing goals of care	50
7. End-of-life counseling	51
8. Counseling for terminally ill patients	52
9. Death confirmation & death certification	53
10. Requesting investigations for histopathology of specimen after procedure	54
11. Medical certificate	54
12. Consultation request form	55
13. Discharge planning & patient summary	56
14. Hospital discharge summary form	57
15. Taking consent for DAMA/LAMA	58
CHAPTER-5 INFECTIOUS DISEASES	
1. Fever of unknown origin (FUO)	59
2. Fever with chills and rigors	60
3. Sepsis	61
4. Typhoid fever (Enteric fever)	63
5. Malaria fever	64
6. Dengue fever	66
7. Brucellosis	69
8. Weil's Disease (Leptospirosis)	70
9. Schistosomiasis	71
10. Leishmaniasis	72
11. Scrub typhus (tick typhus)	74
12. Epidemic typhus	74
13. Endemic typhus (murine typhus)	75
14. Rocky mountain spotted fever	75
15. Coxiella Burnetii (Questionable "Q" Fever)	76
16. Trichuriasis (whipworm)	76
17. Fish tapeworm infection (Diphyllobothrium latum)	77
18. Hookworm infections (Ancylostoma duodenale)	77
19. Enterobiasis (Pinworm)	78
20. Ascariasis (Giant roundworm)	78
21. Cutaneous larva migrans (Creeping eruption)	79
22. Lymphatic filariasis	79
23. Lymphogranuloma venereum (LGV)	80
24. Genitourinary chlamydia (Non-lymphogranuloma venereum)	81
25. Granuloma inguinale (Donovanosis)	82
26. Chancroid	83
27. Herpes genitalis (Cold or Fever sore)	84
28. Urogenital gonococcal (gonorrhea) infections	85
29. Syphilis	86
30. Bacillary dysentery (Shigellosis)	87
31. COVID-19 (Coronavirus disease 2019)	88
CHAPTER-6 PULMONOLOGY	
1. Fever with dry cough	95
2. Fever with productive cough	95
3. Community-acquired pneumonia (CAP) - outpatient (OPD)	96
4. Community-acquired pneumonia (CAP) - inpatient (ward)	98
5. Hospital-acquired (nosocomial) pneumonia	99
6. Ventilator-associated pneumonia (VAP)	100
7. Chlamydia psittaci pneumonia	101
8. Mycoplasma pneumonia	101
9. Legionella pneumonia (legionnaires disease/legionellosis)	102
10. Staphylococcal pneumonia	102
11. Lung abscess	103
12. Pulmonary tuberculosis (PTB)	104
13. Anti-tubercular drugs	106
14. Bronchial asthma	107
15. Chronic obstructive pulmonary disease (COPD)	110
16. Severe cough in a patient with history of asthma	113
17. Pleural effusion	114
18. Sarcoidosis	116
19. Bronchiectasis	117
20. Evaluation of carcinoma lung (Bronchogenic carcinoma)	119
21. Commonly used medications in respiratory diseases	120
22. Commonly used anti-tussive/cough suppressant	122
CHAPTER-7 CARDIOVASCULAR DISEASES (CVS)	
1. Evaluation to the management of hypertension	123
2. Choice of anti-hypertensive medication	125

3. Strategies for initial management of hypertension	126
4. Hypertension (HTN) – Medication prescription	127
5. Anti-hypertensive treatment based on comorbid	128
6. HTN long-term management & follow-up	129
7. ST-Segment elevation myocardial infarction (STEMI)	130
8. Stable angina pectoris	132
9. Un-stable angina/NSTEMI	134
10. Congestive cardiac failure (CHF)	135
11. Approach to the diagnosis of heart failure (HF)	137
12. Medical treatment of HF according to stages	138
13. General measure and approach to the management of heart failure	139
14. Evidence-based treatment of heart failure	140
15. Treatment of Heart Failure with Reduced Left Ventricular EF (HFrEF)	140
16. Treatment of Heart Failure with Preserved Left Ventricular EF (HFpEF)	141
17. Acute heart failure (AHF)	142
18. Infective endocarditis (IE)	145
19. Acute rheumatic fever and Rheumatic heart disease (RHD)	148
20. Pericarditis	149
21. Pericardial effusion and cardiac tamponade	152
22. Cardiomyopathies	155
23. Dilated cardiomyopathy (DCM)	155
24. Hypertrophic cardiomyopathy	157
25. Restrictive cardiomyopathy (RCM)	159
26. Commonly used medications in cardiovascular diseases (CVD)	161

CHAPTER-8 GASTROENTEROLOGY

1. Management nausea &/or vomiting	165
2. Life-threatening causes of nausea & vomiting	166
3. Aphthous stomatitis (oral ulcer/canker sore)	167
4. Oral thrush (oropharyngeal candidiasis)	168
5. Gastro-esophageal reflux disease (GERD)	169
6. Peptic ulcer (Gastric ulcer & Duodenal ulcer)	170
7. Helicobacter pylori (H. pylori) infection	171
8. Functional dyspepsia	173
9. Clostridioides (Clostridium) difficile colitis	174
10. Hiccups (Singultus)	175
11. Irritable bowel syndrome (IBS)	177
12. Ulcerative colitis (UC)	178
13. Crohn disease (CD)	181
14. Celiac disease	183
15. Malabsorption	185
16. Small intestinal bacterial overgrowth (SIBO)	186
17. Adults constipation	187

CHAPTER-9 HEPATOLOGY

1. Approach to the jaundice & cholestasis	189
2. Hepatitis-A virus (HAV) Infection	192
3. Chronic Hepatitis-B viral (HBV) Infection	193
4. Chronic Hepatitis-C viral (HCV) Infection	197
5. Non-alcoholic fatty liver disease (NAFLD) OR (Fatty liver/Hepatic steatosis)	199
6. Ascites	200

7. Decompensated chronic liver disease (DCLD) = Liver Cirrhosis + Ascites	202
8. Primary biliary cholangitis (PBC)	203
9. Amoebic liver abscess	204
10. Hemochromatosis (Iron overload disease)	205
11. Wilson's disease	207
12. Acute liver failure (ALF)	208

CHAPTER-10 ENDOCRINOLOGY

1. Diabetes mellitus (DM) – Diagnostic approach	211
2. Diabetes mellitus type-1 (T1DM)	212
3. Insulin – antidiabetics/anti-hyperglycemic drugs	214
4. Characteristics of insulin therapy	214
5. Diabetes mellitus type-2 (T2DM)	215
6. Diabetic kidney disease (DKD)/Diabetic nephropathy	219
7. Diabetic neuropathy	221
8. Diabetic retinopathy	224
9. Non-insulin antidiabetics/anti-hyperglycemic drugs	225
10. Insulin regimens	227
11. Sliding-scale insulin regimen	228
12. Insulin regimens for Glucocorticoid-Induced Hyperglycemia	228
13. Diabetic ketoacidosis (DKA)	229
14. Hyperosmolar hyperglycemic state (HHS)	231
15. Hypothyroidism	233
16. Hyperthyroidism & thyrotoxicosis	234
17. Pheochromocytoma	235
18. Hyperprolactinemia	237
19. Acromegaly	238
20. Cushing syndrome (hypercortisolism)	239

CHAPTER-11 NEPHROLOGY & UROLOGY

1. Urinary tract infection (UTI)	243
2. Acute pyelonephritis	244
3. Nephrolithiasis (Renal stones)	246
4. Radiological interpretation of nephrolithiasis	247
5. Benign prostatic hyperplasia (BPH)	249
6. International prostate symptom score (IPSS)	249
7. Urinary incontinence	251
8. Treatment of Urge urinary incontinence	253
9. Treatment of Stress urinary incontinence	253
10. Treatment of Overactive bladder (OAB)	253
11. Treatment of Overflow incontinence	253
12. Male sexual dysfunction & erectile dysfunction	254
13. Nephritic syndrome	256
14. Nephrotic syndrome	257
15. Acute renal injury (AKI)	258
16. Diagnostic finding in different types of AKI	260
17. Treatment for the underlying cause of AKI	261
18. Treatment of Acute renal injury (AKI)	262

CHAPTER-12 HAEMATOLOGY

1. Iron deficiency anemia (IDA)	263
2. Megaloblastic anemia	265
3. Vitamin B12 deficiency anemia	265
4. Folic Acid deficiency anemia	265
5. Diagnosis of megaloblastic anemia	266

6. Treatment of megaloblastic anemia	267	3. Panic attack	353
7. Acute leukemia	268	4. Panic disorder	353
8. Thrombotic thrombocytopenic purpura (TTP)	271	5. Generalized anxiety disorder (GAD)	354
9. Immune thrombocytopenic purpura (ITP)	272	6. Major depressive disorder (MDD)	355
10. Hemophilias	274	7. Obsessive-compulsive disorder (OCD)	348
11. Aplastic anemia	276	8. Bipolar affective disorder (BIPAD)	359
12. Thalassemias	278	9. Schizophrenia	362
13. Glucose-6-phosphate dehydrogenase (G6PD) deficiency	280	10. Opioid use disorder (OUD)	364
14. Sickle cell anemia	281	11. Conversion disorder	365
15. Disseminated intravascular coagulation (DIC)	283		
CHAPTER-13 RHEUMATOLOGY		CHAPTER-16 DERMATOLOGY	
1. Osteoporosis	287	1. Scabies	367
2. Post-menopausal osteoporosis	288	2. Acne vulgaris	368
3. Arthritis	289	3. Seborrheic dermatitis (Seborrheic eczema)	370
4. Post-chikungunya arthritis	289	4. Psoriasis	371
5. Osteoarthritis	290	5. Tinea capitis	374
6. Rheumatoid arthritis	293	6. Tinea pedis (Athlete's foot) & Tinea manuum	375
7. Gouty arthritis & Hyperuricemia	297	7. Tinea cruris (Jock itch)	375
8. Systemic lupus erythematosus (SLE)	300	8. Tinea corporis (Body ring worm)	376
9. Lupus nephritis	304	9. Tinea varicolor (Pityriasis varicolor)	377
10. Plantar fasciitis	305	10. Tinea unguium (Onychomycosis/Fungal nail)	378
11. Polymyalgia rheumatica	305	11. Pityriasis rosea	379
12. Giant cell arteritis (Temporal arteritis)	306	12. Melasma	380
13. Psoriatic arthritis (PsA)	308	13. Vitiligo	381
14. Reactive arthritis (Reiter syndrome)	310	14. Herpes-zoster (Shingles)	383
15. Septic arthritis	312	15. Atopic dermatitis/Atopic eczema	384
16. Fibromyalgia (FM) syndrome	314	16. Allergic contact dermatitis	385
17. Frozen shoulder (Adhesive capsulitis)	316	17. Diaper dermatitis (Nappy dermatitis)	386
		18. Pompholyx (Dyshidrotic eczema)	387
CHAPTER-14 NEUROLOGY		19. Hyperhidrosis	388
1. Migraine headache	317	20. Hirsutism	389
2. Status migrainosus	712	21. Androgenetic alopecia	390
3. Cluster headache	319	22. Alopecia areata	391
4. Tension type headache	320	23. Telogen effluvium (Excessive hair shedding)	392
5. Transient ischemic attack (TIA)	321	24. Burn	393
6. Ischemic stroke (Cerebral infarction/CVA)	322	25. Stevens-johnson syndrome (SJS)	397
7. Post-herpetic neuralgia (PHN)	325	26. Sunburn	401
8. Trigeminal neuralgia (5 th CN Palsy)	326	27. Commonly used dermatological (skin) drugs	402
9. Bell's palsy (Facial/7 th CN palsy)	327		
10. Parkinson's disease (PD)	329	CHAPTER-17 GENERAL SURGERY	
11. Resting tremor	331	1. Approach to management of acute abdomen	409
12. Essential tremor	332	2. Differential diagnosis and causes of acute abdomen	415
13. Alzheimer's disease (AD)	333	3. Diagnostic approach of acute abdomen	416
14. Myasthenia gravis (MG)	336	4. Radiological approach of acute abdomen	417
15. Guillin-barre syndrome (GBS)	338	5. Stepwise management of acute abdomen	418
16. Multiple sclerosis (MS)	340	6. Acute appendicitis	419
17. Cerebral palsy (CP)	656	7. Acute cholecystitis	420
18. Seizures & Epilepsy (Seizure disorders)	345	8. Cholelithiasis (Gallstones)	422
19. Guidelines for antiepileptic medication therapy	347	9. Choledocolithiasis	423
20. Characteristics of commonly used antiepileptic drugs in adults	348	10. Acute cholangitis	424
21. Long term treatment prescription of epilepsy/seizures	349	11. Anal fissure	426
		12. Hemorrhoids	427
CHAPTER-15 PSYCHIATRY		13. Ano-rectal abscess	428
1. Insomnia disorder	351	14. Pilonidal sinus	428
2. Acute stress disorder	352	15. Acute pancreatitis	429
		16. Intestinal (Bowel) obstruction	432
		17. Spontaneous bacterial peritonitis	433
		18. Secondary bacterial peritonitis	434

19. Pressure ulcer (decubitus ulcer, bed sore)	435
20. Diabetic foot infections	437
21. Hypertrophic scar	438
22. Keloids	439
23. Lipoma	440
24. Skin tag (Acrochordon)	440
25. Ganglionic cyst	441
26. Ingrown toe-nail	442
27. Felon finger infection	442
28. Acute paronychia	443
29. Chronic paronychia	443

CHAPTER-18 OPHTHALMOLOGY (EYE)

1. Hordeolum (Stye)	445
2. Chalazion (Meibomian gland lipogranuloma)	445
3. Iritis (Anterior uveitis)	446
4. Acute mucopurulent conjunctivitis	446
5. Chlamydial conjunctivitis	447
6. Allergic conjunctivitis	447
7. Viral conjunctivitis (Adenovirus conjunctivitis)	448
8. Herpes simplex keratitis	449
9. Blepharitis (Blepharitis squamosa)	450
10. Corneal abrasion	451
11. Sub-conjunctival hemorrhage	451
12. Ocular chemical burns injuries (Non-mechanical)	452
13. Corneal foreign bodies (Mechanical)	453
14. Acute angle closure glaucoma (AACG)	454
15. Ophthalmic (Eye) drug brands	456

CHAPTER-19 ENT

1. Acute tonsillitis & pharyngitis	459
2. Acute sinusitis (Acute rhino-sinusitis)	461
3. Chronic sinusitis (Chronic rhino-sinusitis)	462
4. Non-allergic rhinitis (NAR)	463
5. Chronic simple rhinitis	464
6. Hypertrophic rhinitis (Chronic)	464
7. Allergic rhinitis	465
8. Deviated nasal septum (DNS)	466
9. Septal haematoma	467
10. Septal abscess	467
11. Nasal turbinate hypertrophy	468
12. Adult with ear discharge/Infection	468
13. Acute suppurative otitis media (ASOM)	469
14. Chronic suppurative otitis media (CSOM)	470
15. Otitis externa and its classification	472
16. Localized acute otitis externa (furunculosis)	472
17. Diffuse otitis externa	473
18. Malignant (Necrotizing) otitis externa	474
19. Otomycosis (Fungal otitis externa)	475
20. Herpetic otitis externa	475
21. Ear wax (Cerumen impaction)	476
22. Tinnitus	477
23. Vertigo	478
24. Benign paroxysmal positional vertigo (BPPV)	479
25. Ear, nose and throat (ENT) drug brands	481

CHAPTER-20 NEURO-SPINE SURGERY

1. Approach to degenerative disk diseases	485
2. Red flags features for acute back pain	486

3. Management and evaluation of degenerative disk diseases	486
4. MRI Anatomy of the cervical & lumbar spine	487
5. Treatment approach of degenerative disk diseases	488
6. Cervical radiculopathy (Brachialgia/pinched nerve)	489
7. Lumbosacral radiculopathy	490
8. Low back pain	491
9. Sciatica pain	493
10. Spinal stenosis	494
11. Epidural (Extra-dural) hematoma (EDH)	496
12. Subdural hematoma (SDH)	498
13. Subarachnoid hemorrhage (SAH)	501
14. Brain abscess	502
15. Hydrocephalus	504
16. Cerebral shunt (Ventriculoperitoneal shunt)	505
17. Cervical spine distortion (whiplash injury)	505
18. Traumatic brain injury (Head trauma)	506
19. Pneumocephalus (Intracranial aerocele)	507

CHAPTER-21 GYNAECOLOGY & OBSTETRICS

1. Fever with dry cough (acute) in pregnancy	509
2. Fever with productive cough in pregnancy	509
3. Typhoid fever (Enteric Fever) in pregnancy	510
4. Malaria (Falciparum malaria) in pregnancy	511
5. Urinary tract infection (UTI) in pregnancy	512
6. Nephrolithiasis (Renal stones) in pregnancy	513
7. Pneumonia OPD treatment in pregnancy	514
8. Pneumonia, inpatient (WARD) in pregnancy	515
9. Hepatitis-B viral (HBV) infection in pregnancy	516
10. Vaginal yeast infection (vulvo-vaginal candidiasis)	517
11. Chlamydial infections in women's	517
12. Leukorrhea	518
13. Pelvic inflammatory diseases (PID)	519
14. Vaginal trichomoniasis	520
15. Candida vaginitis (moniliasis)	521
16. Bacterial vaginosis	521
17. Bartholinitis (infections of Bartholin's gland)	522
18. Bartholin's abscess	522
19. Pelvic abscess	523
20. Atrophic vaginitis (Senile vaginitis)	524
21. Primary dysmenorrhea (Menstrual pain)	524
22. Secondary dysmenorrhea	525
23. Premenstrual syndrome (PMS)	526
24. Mittelschmerz's syndrome (Ovulatory pain)	527
25. Menorrhagia	527
26. Oligomenorrhea	527
27. Endometriosis	528
28. Uterine fibroids (Uterine leiomyomas)	531
29. Female infertility	532
30. Polycystic ovary syndrome (PCOS)	534
31. Ovarian cyst (Benign)	537
32. Follicular cyst	537
33. Post-partum hemorrhage (PPH)	538
34. Nausea & vomiting of pregnancy (NVP)	540
35. Hyperemesis gravidarum	540
36. Chronic hypertension in pregnancy	541

37. Pre-Eclampsia	542
38. Eclampsia	546
39. Acute fulminant pre-eclampsia	546
40. Epilepsy in pregnancy	547
41. Migraine headache in pregnancy	548
42. Menstrual migraine	548
43. Gastroesophageal reflux disease (GERD) in pregnancy	549
44. Peptic ulcer disease (PUD) in pregnancy	549
45. Helicobacter pylori in pregnancy	550
46. Constipation in pregnancy	550
47. Iron deficiency anemia (IDA) in pregnancy	551
48. Megaloblastic anemia (MBA) in pregnancy	552
49. Gestational diabetes mellitus (GDM)	553
50. Hypoglycemia in pregnancy	554
51. Diabetic Ketoacidosis (DKA) in pregnancy	555
52. Hyperthyroidism/Thyrotoxicosis in pregnancy	556
53. Hypothyroidism in pregnancy	557
54. Normal pregnancy	558
55. Pregnancy – Pre-conception counselling	559
56. Diagnosis of pregnancy – clinical guidelines	561
57. Beta-HCG and its overview	561
58. Physiological changes during pregnancy	562
59. Nutrition during pregnancy	564
60. Physical activity during pregnancy	565
61. Safe and unsafe sports during pregnancy	565
62. High-risk pregnancy	565
63. RH incompatibility	566
64. Ectopic pregnancy	568
65. Spontaneous abortion	571
66. Types of spontaneous abortion/pregnancy loss	571
67. Recurrent or Habitual miscarriage	573
68. Induced abortion (Termination of a pregnancy)	575
69. The Islamic teachings about abortion	575
70. Abortion laws in Pakistan	575
71. Ethics in abortion	576
72. Medical termination of pregnancy – RCOG, ACOG, WHO Guidelines	577
73. Anti-phospholipid syndrome (APS)	576
74. Puerperal sepsis	579
75. Postpartum endometritis	580
76. Emergency contraception "postcoital contraception"	581
77. Overview of different types of hormonal contraceptives	582
78. Gynae & Obs drug brands in Pakistan	583
79. U.S. Food and drug administration pregnancy drug categories, 1979	587
80. Drugs used in pregnancy with known adverse effects in human pregnancy	587
81. Safe medicines in Pregnancy	588
82. World health organization general cautions for drugs and breast feeding	591
83. 2015-US Food & drug administration pregnancy and lactation labeling rule required information on package insert for every medication	591
84. Fetal radiation effects & characteristics	592

CHAPTER-22 PAEDIATRICS & NEONATOLOGY

1. The newborn infant	593
2. Apgar score	593
3. Neonatal resuscitation	594
4. Assessment of the newborn	595
5. Paediatric intravenous (IV) fluid prescribing	596
6. Neonatal hypothermia	596
7. Vitamin-K deficiency bleeding of the newborn	599
8. Neonatal polycythemia	599
9. Neonatal hypocalcemia	600
10. Neonatal hypoglycemia	601
11. Neonatal respiratory distress syndrome (NRDS)	601
12. Surfactant replacement therapy (Guidelines)	604
13. Less invasive surfactant administration (LISA)	605
14. Neonatal jaundice	606
15. Guidelines for phototherapy and exchange transfusion	607
16. Neonatal seizures	608
17. Neonatal sepsis	609
18. Omphalitis (Umbilical sepsis)	610
19. Acute tonsillitis	611
20. Acute epiglottitis	612
21. CROUP (Laryngotracheobronchitis)	613
22. Bronchiolitis	615
23. Lower respiratory tract infections (LRTIs)	616
24. Community acquired pneumonia (CAP) – OPD	617
25. Paediatric pneumonia (CAP) inpatient-Ward	618
26. Acute asthma in children's	619
27. Status asthmaticus in children's	620
28. Child with cold & flu	620
29. Allergic rhinitis	621
30. Child with dental infection	622
31. Child with ear pain	622
32. Child with ear discharge/infection	623
33. Dental infections in children	623
34. Acute suppurative otitis media (ASOM)	624
35. Management of fever	625
36. Enteric fever (Typhoid fever)	627
37. Malaria fever	628
38. Childhood tuberculosis (TB)	629
39. Chickenpox (Varicella)	631
40. Mumps (Epidemic parotitis)	632
41. Measles (Rubeola)	633
42. Subacute sclerosing panencephalitis (SSPE)	634
43. H. Pylori infection	634
44. Urinary tract infection (UTI) in children and adolescents	635
45. Iron deficiency anemia (IDA)	636
46. PICA eating syndrome	636
47. Vitamin-D Deficiency	636
48. Infantile colic	637
49. Constipation	638
50. Dehydration	640
51. Assessment of dehydration	640
52. Acute diarrhea	641
53. Bacillary dysentery (Shigellosis)	642
54. Lactose intolerance	643
55. Hypocalcaemia	643

56. Status epilepticus	644	23. Iron deficiency anemia (IDA)	700
57. Febrile seizures	645	24. Megaloblastic anemia	700
58. Long term treatment of chronic epilepsy or seizures	647	25. Acute bronchial asthma	701
59. Characteristics of commonly used antiepileptic drugs in children's	648	26. Treatment of Status asthmaticus	701
60. Long term treatment of epilepsy/seizures	648	27. Acute exacerbation of chronic obstructive pulmonary disease (AECOPD)	702
61. Treatment of partial (focal) seizures	649	28. Acute renal colic (acute renal pain)	702
62. Treatment of generalized tonic-clonic (GTCS)	649	29. Acute pyelonephritis	703
63. Treatment of childhood typical absence epilepsy	649	30. Cardiac arrest	704
64. Treatment of typical absence, myoclonic, or atonic epilepsy	649	31. Myocardial infarction/STEMI	706
65. Bacterial meningitis	650	32. Pulmonary edema	708
66. Acute rheumatic fever & rheumatic heart disease (RHD)	652	33. Pulmonary embolism	709
67. Hypothyroidism	653	34. Fever with altered level of consciousness (ALOC)	711
68. Hyperthyroidism & thyrotoxicosis	654	35. Status migrainosus	712
69. Autism spectrum disorder (ASD)	655	36. Bacterial meningitis	713
70. Cerebral palsy (CP)	656	37. Viral meningitis	714
71. Bell's palsy (facial nerve paresis/7th CN paralysis) in children's	657	38. Tuberculous meningitis (TBM)	715
72. Poststreptococcal glomerulonephritis (PSGN)	658	39. Encephalitis	716
73. Scabies	659	40. Ischemic stroke (cerebral infarction/CVA)	717
74. Impetigo	660	41. Intracerebral hemorrhage (ICH)/intraparenchymal hemorrhage	720
75. Dog bite (rabies virus) in children's	661	42. Anaphylaxis	723
76. Tetanus	662	43. Benzodiazepines poisoning	723
77. Prevention of tetanus	663	44. Approach to the poisoned or overdose patients	724
78. Immunization schedule in children's	664	45. Organophosphate (OP) poisoning	727
79. IV Paediatrics dosages quick chart	665	46. Opioid overdose (opioid toxicity)	728
80. Oral Paediatrics dosages quick chart	667	47. Paracetamol (acetaminophen) overdose	729
CHAPTER-23 EMERGENCY MEDICINE & POISONING		48. Amphetamines overdose	730
1. The primary and secondary surveys	671	49. Cocaine overdose	732
2. FAST (= focused assessment with sonography for trauma)	672	50. Corrosive poisons (acids/caustic ingestion)	734
3. Approach to the management of pain	673	51. Kerosene poisoning	735
4. Oral opioid & non-opioid analgesics	675	52. Paraphenylene diamine (PPD) poisoning (Kala-Pathar poisoning)	736
5. Foreign body aspiration (FBA)	677	53. Wheat pill poisoning (rice pill poisoning)	737
6. Evaluation & management of comatose patient	681	54. Human bites	739
7. Glasgow coma scale (GCS)	681	55. Insect bites/Sting bites	739
8. Treatment approach to the comatose patient	682	56. Dog bites (Rabies virus)	740
9. Treatment of acute diarrhea in adults	684	57. Snake bites	741
10. Acute infectious gastroenteritis (food poisoning)	685	58. Cat bites	742
11. Bacillary dysentery (Shigellosis)	686	59. Hypokalemia	743
12. Typhoid fever (Enteric fever)	687	60. Hyperkalemia	744
13. Severe falciparum malaria	688	61. Hypoglycemia	745
14. Acute hepatitis-A virus (HAV) infection	689	62. Heat stroke	746
15. Epistaxis (bleeding through nose)	690	CHAPTER-24 PAKISTAN - COMMON DRUG BRANDS	
16. Hypovolemic shock	693	1. NSAIDs, Antipyretics, opioids analgesic	749
17. Upper gastrointestinal (GI) bleed	695	2. Antibiotics	751
18. Hepatic encephalopathy	696	3. Anti-depressants	753
19. Acute haemolytic transfusion reaction	697	4. Benzodiazepines/Tranquilizer/anti-anxiety	755
20. Amoebic liver abscess	697	5. Anti-epileptic/anticonvulsive	756
21. Pyogenic liver abscess	698	6. Anti-Psychotics	757
22. Dengue fever with severe/Progressive thrombocytopenia	699	7. Anti-Allergic/antihistamine	758
		8. Anti-Emetic/Anti-Vertigo	759
		9. Anti-peptic ulcer and GERD	760
		10. Anacid/antiflatulants/antispasmodic	761
		11. Laxative (stool softeners)	762
		12. Muscle relaxant	762
		13. Multivitamins/iron & supplementation	763
		14. Anti-Viral	766

PRINCIPLES FOR EFFECTIVE CLINICAL DIAGNOSIS

➤ There are three main steps to making a correct diagnosis of the patients:

1. **History taking:** Gather detailed information on medical history, symptoms, and important factors.
2. **Physical Examination:** Perform a comprehensive physical exam to observe for signs of illness.
3. **Diagnostic investigation:** Select & interpret test wisely based on clinical suspicion and findings.

SIGNIFICANT OF HISTORY TAKING

- Obtaining an accurate history is the crucial initial stage in identifying the cause of a patient's issue.
- It allows doctors to make accurate provisional diagnosis.

GENERAL APPROACH TO PATIENT INTERACTION

1. **Introduction and Identification:** Start by introducing yourself with your name and position. Confirm the patient's identity by verifying their name and date of birth.
2. **Establishing Rapport:** Interact in a friendly manner to create a comfortable environment.
3. **Seeking Permission:** Obtain consent before discussing the patient's concerns or symptoms.
For example: "Is it okay if I ask you some questions about your cough?"
4. **Respecting Confidentiality:** Emphasize the importance of confidentiality and respect the patient's privacy at all times. "Keep what the patient tells you private and don't share it with others."
5. **Empathy and Understanding:** Endeavor to empathize with the patient's perspective and emotions. Consider factors such as mental status, anxiety, or depression that may influence their presentation.
6. **Optimal Positioning:** Ensure both you and the patient are positioned comfortably for communication. Situate yourself at the same level as the patient, maintaining an appropriate distance, and avoiding barriers such as desks.
7. **Active Listening:** Practice active listening skills, allowing the patient to express themselves fully without interruption. "Pay attention and don't interrupt when the patient is talking."
8. **Empathize with the patient's perspective:** Try to see things from the patient's point of view.
9. **Effective Questioning:** Ask clear and simple questions using language that the patient can understand. Avoid medical jargon and use open-ended questions to encourage dialogue. Summarize key points to ensure mutual understanding.

COMPONENTS OF HISTORY TAKING

1. PERSONAL DETAILS:

Name:	اپکا پورا نام کیا ہے؟
Age:	آپ کی عمر کتنی ہے؟
Gender:	مریض کو دیکھنے سے پتہ چل جائے گا۔
Address:	آپ کہاں رہتے ہیں؟
Occupation	آپ کام کیا کرتے ہیں؟
Religion	—
Marital status	کیا آپ شادی شدہ ہیں؟
Date of Admission	آپ ہسپتال کب تشریف لائے؟ / آپ ہسپتال کس وقت آئے تھے؟
Mode of Admission	آپ اوپی ڈی میں آئے تھے یا ایمرجنسی میں؟

2. CHIEF COMPLAINT (C/C):

1. This is why the patient is here, in the emergency or outpatient department (OPD)

What brings you here? "جی آپ کس مسئلے (تکلیف) کے ساتھ ہسپتال آئے ہیں؟"

How can I help you? "میں آپ کی کس طرح مدد کر سکتا ہوں؟"

What seems to be bothering you? "آپ کو کیا تکلیف ہو رہی ہے؟"

2. This must be put in a short statement in the patient's own words.
3. If there are more than one complaint, list them in order of severity or duration.
4. Include the duration of the chief complaint.
5. Each complaint should be written in one line.

➤ For example: (It should be recorded in patient own words)

Chief Complaint (Symptoms)	Duration
• Fever	4 days
• Cough	3 days
• Sputum production/Expectoration	2 days
• Presence of blood in sputum	1 day

3. HISTORY

1) History of present illness:

➤ This is the detailed explanation of why the patient is seeking medical attention, encompassing the 'why, when, and where' of their symptoms.

➤ **OD-PARA Approach:** Using the OD-PARA approach can help in developing a comprehensive understanding to cover all aspects of information and differential diagnosis.

1. **Onset:** Determine when the chief complaint began, noting whether it was gradual, rapid, sudden, intermittent, or constant.

2. **Duration:** Inquire about the timing of symptoms, such as whether they occur at specific times of day (e.g., night, morning) and their overall duration.

3. **Progression:** Assess whether the problem is worsening, improving, or staying the same. Explore factors that may exacerbate or alleviate the symptoms.

4. **Aggravating factor:** Identify any triggers or activities that worsen the symptoms, such as certain foods or behaviors.

5. **Relieving factor:** Determine if there are any interventions or behaviors that alleviate the symptoms, such as consuming specific foods or adopting particular positions.

6. **Associated symptoms:** Inquire about any additional symptoms or related information not previously discussed, such as nausea or vomiting.

➤ By employing this structured approach, clinicians can gather comprehensive information, leading to a more accurate diagnosis and tailored treatment plan.

➤ **Example OF OD-PARA in Urdu is:**

O- Onset:	جی آپ کو بخار کیسے شروع ہوا؟
D- Duration:	آپ کو بخار کب سے ہے؟
P- Progression:	شروع ہونے کے بعد بخار اب تک کیسے چل رہا ہے؟
A- Aggravating factor:	کسی وجہ سے بخار بڑھ جاتا ہو؟
R- Relieving factor	کسی وجہ سے بخار کم ہو جاتا ہو؟
A- Associated features:	بخار کے ساتھ آپ نے کوئی اور مسئلہ بھی محسوس کیا ہے؟ بخار کے علاوہ کیا آپ نے کوئی اور تکلیف بھی محسوس کیا ہے؟ مریض: کھانسی ہے، بلغم ہے، چھاتی میں درد ہے۔

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➤ For pain SOCRATES approach "A useful mnemonic = SOCRATES"

1. **Site:** where exactly is the pain?
2. **Onset and progression:** when did the pain start and how has it changed or evolved?
3. **Character:** what type of pain is it (e.g. dull, sharp, or crushing)?
4. **Radiation:** does the pain move anywhere (e.g. into the jaw, arm, or back)?
5. **Associated symptoms and signs:** ask specifically about sweating, nausea and vomiting, shortness of breath, cough, haemoptysis, dizziness, and palpitations
6. **Timing and duration:** does the pain occur at particular times of the day? How long does each episode last?
7. **Exacerbating and alleviating factors:** does anything make the pain better or worse (e.g. exercise, movement, deep breathing, coughing, cold air, large or spicy meals, alcohol, rest, GTN, sitting up in bed)?
8. **Severity:** "How would you rate the pain on a scale of 1 to 10, with 1 being no pain at all and 10 being the worst pain you have ever experienced?"



2) PAST MEDICAL HISTORY

- Ask the patient about all previous medical issues the patient has experienced.
- Patients may recall these issues accurately or may forget some. To ensure comprehensive assessment, specifically ask about the following significant conditions:

Mnemonic: "MJTHREADS Ca"

✚ Myocardial infarction	✚ Jaundice
✚ Tuberculosis	✚ Hypertension
✚ Rheumatic fever	✚ Epilepsy
✚ Asthma	✚ Diabetes
✚ Stroke	✚ Cancer (and treatment if so)

- ❖ By addressing past medical history in this manner, healthcare providers can obtain a thorough understanding of the patient's medical background, facilitating better-informed clinical decision-making and management.

3) DRUG HISTORY

- Ask about all medications the patient is currently taking.
- For each medication, find out:
 - ✚ How much they take.
 - ✚ How often they take it.
 - ✚ How they take it (e.g., by mouth, injection)
 - ✚ If they take it regularly
- For medications taken weekly, ask which day they take it.
- For drugs with changing doses (like Warfarin), ask what their current dose is.
- Ask about any recreational drug use, including injecting drugs.
- Ask about any over the counter (OTC) medications they use.
- ❖ This information helps doctors make sure patients take their medications safely and get the right treatment.

4) ALLERGIES HISTORY

- 
- Ask the patient if they have any allergies.
 - If they are allergic to medications, find out which medication they are allergic to and what reaction they had.
 - **For example**, reactions to medications like Sulfa drugs may cause a rash, Cipro may cause a rash, and Benadryl may cause a mild dystonic reaction.
 - Specifically ask if there has been a history of anaphylaxis, which includes symptoms such as throat swelling, trouble breathing, or a puffy face.
 - ❖ This information helps ensure patient safety by avoiding medications that could cause harmful allergic reactions.

5) FAMILY HISTORY

- Ask the patient about any family diseases related to their current health concerns. For example, if the patient is experiencing chest pain, inquire about a family history of MI/heart attacks.
- Ask about the health of the patient's parents and siblings. If any of them passed away before the age of 65, ask about the cause of death.
- If relevant and if a pattern has emerged from previous history, sketch a brief family tree to visualize the familial health connections.
- ❖ Understanding the patient's family medical history helps healthcare providers assess potential genetic predispositions and tailor preventive measures and treatment plans accordingly.

6) SOCIAL HISTORY:

- **Occupation/Employment:** Ask about their job, "What do you do for work? Have you been around anything that might be harmful, like asbestos?" Occupations linked to asbestos exposure include construction, shipyard, industrial, insulation, and mining workers.
- **Marriage Status:** Ask about their marital status. "Are you married?"
- **Tobacco Use:** Find out how much and for how long they've smoked. Ask how many cigarettes do you smoke each day, and for how many years have you been smoking?
Calculate pack years (number of packs smoked per day multiplied by years of smoking).
- **Alcohol Use:** Determine how many units of alcohol they consume per week.
- **Illicit Drug Use:** "Have you ever used any illegal drugs?"
- **Immunization Status:** Check if they've had recent vaccinations.
- **Home Situation:** Tell me about where you live, who takes care of you, what you do every day, how you get around, and who helps you out when you need it.
- **Travel History:** Ask about recent travel, especially if it relates to their current health concern. "Have you been anywhere recently? Have you traveled anywhere, especially somewhere that might be connected to why you're here?"
- **Depending on the complaint:**
 - ✎ **Respiratory Issues:** Inquire about pets, dust exposure, farming, bird exposure, or hobbies.
 - ✎ **Infectious Diseases:** Ask about sexually transmitted diseases, full travel history, water exposure, foreign food exposure, tuberculosis, and HIV risk factors.
- ❖ This information helps healthcare providers understand the patient's lifestyle and potential environmental exposures that may impact their health.

4. PATIENT GESTURES:

➤ Certain gestures can help identify specific pain symptoms:

- Squeezing the chest may indicate cardiac pain.
- Holding the flank or kidney area suggests renal colic.
- Rubbing the chest bone may indicate heartburn.
- Rubbing the buttock and thigh could suggest sciatica.
- Clasping the arms around the abdomen may indicate mid-gut colic.
- Pressing or applying pressure to the lower right abdomen, often with a grimace or wincing expression, indicates pain localized to the area around the appendix.
- Pressing or holding the temples may indicate a headache or migraine.
- Pressing or tapping on the area around the cheeks or forehead, particularly near the eyes and nose, to indicate sinus pain or pressure.
- Clutching the lower abdomen could suggest gastrointestinal discomfort or menstrual cramps.
- Grasping or massaging the lower back might indicate lower back pain or kidney issues.
- Holding or rubbing the throat may suggest throat pain or difficulty swallowing.
- Pointing to specific areas of the body with discomfort or tenderness can help localize pain and identify underlying conditions.

❖ These gestures provide valuable clues for diagnosing and understanding the patient's symptoms.

5. PATIENT'S PERCEPTION:

- Inquire about the patient's perception of their symptoms and whether they have dismissed any particular features as unimportant. Patients may overlook certain symptoms or attributes that they deem insignificant, which could be crucial in establishing a diagnosis.
- Perform a systematic review of systems, covering respiratory, cardiovascular, central nervous, urinary, and other systems, to uncover any symptoms relevant to each.

6. SYSTEMATIC REVIEW: Run through a checklist of symptoms from major body systems

- **General:** Assessing appetite, weight, sleep, fever, energy level, swelling, body odor, and posture.
- **Respiratory:** Evaluating cough, sputum, hemoptysis, breathlessness, chest pain, and wheezing.
- **Cardiovascular system (CVS):** Checking for chest pain, palpitations, breathlessness, swelling, leg pain, and dizziness.
- **Central Nervous System (CNS):** Inquiring about orientation, headaches, dizziness, weakness, insomnia, consciousness level, and sensory changes.
- **Gastrointestinal:** Investigating dental problems, heartburn, nausea, vomiting, abdominal pain, bowel habits, jaundice, and appetite changes.
- **Genitourinary:** Asking about urinary symptoms, menstrual history (for women), sexual health, and genital discharge.
- **Musculoskeletal:** Assessing weakness, joint pain, back pain, muscle pain, swelling, joint function, fractures, and mobility.
- **Ear, nose, & throat:** Checking for sore throat, ear or sinus pain, hearing loss and nasal symptoms.
- **Eye:** Inquiring about vision changes, redness, discharge, itching, and bulging.
- **Endocrine:** Evaluating thirst, fatigue, temperature tolerance, hair changes, sweating, weight, appetite, and eye appearance.
- **Integumentary (Skin):** Assessing rashes, lumps, itching, bruising, and skin appearance.



7. PHYSICAL EXAMINATION (PE)

1. GETTING READY FOR THE EXAMINATION



- Set up an optimal environment for the examination.
 - Choose a comfortable and quiet place.
 - Respect privacy: Request others to leave the room as needed for patient comfort and confidentiality. Ask other patients and possibly even family members (depending on patient preference and extent of exam) to leave the room.
 - The patient should be approached from the right side.
- Sanitize hands prior to touching the patient.
- Introduce yourself and your title to the patient and explain the procedure.
- Address the patient by name (if known) throughout the examination.
- Keep the patient informed about the next steps during the examination.
- Examination tools include: Pens, stethoscope, penlight, tongue depressor, reflex hammer, otoscope and ophthalmoscope, if necessary.

2. BASIC METHODS:

Each examining system can be described using the following elements;

1. Inspection (Looking): Visual examination.
2. Palpation (Feeling): Feeling for abnormalities.
3. Percussion (Tapping): Tapping to assess density or resonance.
4. Auscultation (Listening): Listening/Auscultation for sounds.
5. Functional examination: Evaluating movement or functionality.

3. CONSECUTIVE STEPS

Approaches to the physical examination vary greatly and depend on a number of factors. Different doctors may examine patients in different ways. This can depend on things like personal preference, the type of doctor, and the rules of the place where they work. It also depends on why the patient is visiting and what problems they have, their medical history, how often they've been seen before, and how much time is available for the examination.

An example of a complete examination sequence could include:

➤ Ask the patient to be seated:

- Initiating Patient Comfort: Some doctors may start by examining the hands or shaking hands with the patient to enhance their comfort with touch during the examination.
- Head and neck examination.
- Neurological examination.
- Pulmonary examination.
- Possibly musculoskeletal examination (depending on patient concern).

➤ Ask the patient to lie supine:

- The patient should lie with upper body at a 30–45° angle for:
 - Cardiovascular examination
 - Peripheral CNS Examination: Assessing reflexes, muscle tone, and peripheral sensation.
- The patient should lie flat for:
 - Abdominal examination
 - Possibly musculoskeletal examination (depending on patient concern)
 - Breast examination as indicated (inspection should have occurred while seated)
 - Pelvic, prostate, or rectal exams are conducted based on the patient's history or symptoms.



4. GENERAL EXAMINATION:

Evaluate physical, behavioral, and emotional states, including:

- **Physical features and look:** Body type, distinctive features or abnormal formations/symmetry, development, race, hygiene.
- **Notable diagnostic facies** are unique facial features associated with certain specific medical conditions, helping in diagnosis. Examples include:
 - ✦ **Acromegaly:** Enlarged jaw, nose, lips.
 - ✦ **Cushingoid:** "Moon face," buffalo hump.
 - ✦ **Down syndrome:** Upward-slanting eyes, small ears.
 - ✦ **Marfanoid:** Tall stature, long limbs.
 - ✦ **Myxoedematous:** Facial puffiness, dull expression.
 - ✦ **Thyrototoxic:** Weight loss, goiter, exophthalmos.
 - ✦ **Parkinsonism:** Mask-like face, stooped posture.
- **Behavior:** alertness, activity level, lethargic, mood (calm, agitated) and facial expression.
- **Overall wellness:** healthy or unwell
- **Skin coloration:** pink, pale, flushed, jaundiced.
- **Posture and walking pattern** (gait).

5. VITAL SIGNS:

Vitals signs represent key physiological parameters indicating health status. Normal ranges for healthy adults are:

- **Temperature:** 98°F (36.6°C) to 98.6°F (37°C)
- **Respiratory rate (RR):** 12 to 20 breaths per minute
- **Heart rate (Pulse rate):** 60 to 100 beats per minute
- **Blood pressure (BP):** 120/80 mmHg
- **Oxygen saturation (SpO₂):** 94–98%

6. BODY MEASUREMENTS

- **Weight and height:** Indicators of overall size and growth.
- **Body mass index (BMI):** Evaluates weight in relation to height; categories include underweight (<18.5 kg/m²), normal (18.5 – 24.9 kg/m²), and overweight (≥25 – 29.9 kg/m²).
- **Infants & young children:** Head circumference: Assesses head growth and development.

7. SKIN & NAILS EXAMINATION

- **Skin:** Examine skin appearance and lesions, noting their location, size, color, texture, shape, and distribution for accurate documentation
- **Nails:** Inspect (see) and palpate (feel) nails on both fingers and toes, observing for any unusual changes in color, shape, or structure.

8. HEAD, EYES, EARS, NOSE, THROAT (HEENT) EXAMINATION

- **Head, face, and neck:** Inspect (see) and palpate (feel) the head, sinuses, neck, and lymph nodes.
- **Eyes:** Check pupillary response (reactivity to light), eye movements, visual acuity using Snellen chart, and perform fundoscopic examination.
- **Ears:** Inspect (see) and palpate (feel) the ears, perform otoscopic examination, and assess Rinne/Weber tests if necessary.
- **Nose:** Inspect (see) for any deformities or discharge
- **Throat and mouth:** examine throat by asking patient to say "ahh," inspect oral cavity, assess breath/odor, and palpate thyroid gland.

9. LYMPH NODE (LYMPHATICS) EXAMINATION

- Examine different locations such as cervical, axillary, and groin areas.
- **Inspection:** look for visible lymph nodes enlargement
- **Palpate (feels) lymph nodes** for swelling, tenderness, mobility, and irregularity.



10. HEART EXAMINATION

- **Auscultation** of the Aortic, Pulmonic, Tricuspid, Mitral, and carotid areas should be performed directly on the skin, avoiding clothing interference.
- Identify the pulsation of the internal jugular vein.
- **PALPATE PULSES** using the **THREE-FINGER METHOD**, feeling for pulsations with the tips of the 2nd, 3rd, & 4th fingers. **Palpate** the common carotid artery in the neck, radial artery in the wrist, abdominal aorta in the abdomen, femoral artery in the groin, popliteal artery behind the knee, tibialis posterior artery on the inner ankle, and dorsalis pedis artery on the top of the foot.
- **Assess for edema**, distinguishing between pitting (leaving an indentation when pressed) and non-pitting (no indentation) types.
- In cardiovascular examination, percussion and palpation have a limited role, primarily focusing on identifying the point of maximal impulse, heaves, and thrills.

11. LUNGS & CHEST WALL EXAMINATION

- **Inspection:** Observe breathing pattern, thorax shape, and sputum.
- **Palpation:** Check for tenderness, symmetry, & tactile fremitus (ask patient say "ninety-nine").
- **Percussion:** Hyperresonant (excessive air/emphysema) or dull (fluid, pneumonia, or tumors).
- **Auscultate:** would be enough unless there are pulmonary concerns.
- **Perform egophony** by auscultating over the chest & ask patient to say "ee-aa" → lung pathology.

12. ABDOMEN EXAMINATION

- Inspection, Auscultation, Percussion and Palpation
- **Check for signs:** Murphy sign, McBurney, Rovsing sign, Psoas sign, obturator sign
- **Costovertebral angle tenderness:** Pain that is elicited upon percussion of the costovertebral angle (approx. 12th rib). When present, this finding should raise concern for pyelonephritis.

13. PELVIC EXAMINATION

1. Female

- **External genital exam:** check for any abnormalities of the vulva, labia (e.g., swelling, irritation, ulcers)
- **Internal genital exam:** includes the sterile speculum exam, cervicovaginal swab
- **Bimanual pelvic exam:** by introducing two fingers of one hand in the patient's vagina while pressing on the abdomen with the other hand the physician to examine patient's uterus and adnexa (e.g., their localization, size, tenderness during manipulation, presence of masses)
- **Rectovaginal pelvic exam:** allows for the palpation of the rectovaginal septum palpation in patients with suspected pelvic masses (e.g., colorectal cancer)

2. Male

- **Inspection**
 - ↳ Hair pattern or any signs of lice or nits
 - ↳ Presence of circumcision (uncircumcised patients should be examined with the foreskin retracted)
 - ↳ Lesions, rashes, or edema of the penis, scrotum, or perineum
- Palpation of penis, scrotum, and both testicles
- Hernia examination and prostate examination



14. NEUROLOGICAL EXAMINATION

- **Levels of consciousness:** Typically measured by assessing the response to a stimulus (e.g., shouting in the ear, sternal rub) and by the Glasgow coma scale score (eye opening, verbal, and motor responses).
- **Mental status exam**
 - **Orientation to time, place and person:** Person (What is your name?), Time (What is today's date?), Place (What is the name of this place?)
 - **Memory:**
 - » **Short-term memory:** Ask the patient to recall 3 objects after about 2 to 5 min.
 - » **Long-term memory:** Ask the patient a question about the past
 - **Naming objects:** Present an object, such as a pen, book, or ruler, and ask the patient to name the object and a part of it.
 - **Attention and concentration:** Ask the patient to spell a 5-letter word forward and backward. "World" is commonly used.
- **Cranial nerve examination:** Evaluate visual acuity and visual fields (CN II), extraocular movements (CNs III, IV, VI), facial sensation and muscle strength (CN V), facial movements (CN VII), audition (CN VIII), elevation of the soft palate and the uvula (CNs IX, X), trapezius and sternocleidomastoid contraction strength (CN XI), and movement of the tongue. (CN XII). Olfactory examination (CN I) is generally omitted unless relevant to the patient's complaint.
- **Sensory function (pinprick, dull, proprioception)**
- **Motor function (upper motor neuron injury vs. lower motor neuron injury)**
- **Deep tendon reflexes (DTR):** An increased DTR indicates an upper motor neuron issue, whereas decreased DTR indicates a LMN, neuromuscular junction, or muscle issue.
- **Coordination (finger-nose, rapid alternating)**
- **Gait assessment:** Evaluate the patient's ability to stand still, walk naturally, heel walk, toe walk, and tandem walk (heel-to-toe).
- **Romberg test for assessing sensory ataxia** → the patient is asked to stand with both feet together, raise their arms, and close their eyes. The test is positive if closing the eyes impairs coordination (e.g., the patient starts swaying), which is indicative of sensory ataxia. The test is negative if closing the eyes does not affect the patient's balance.
- **Meningeal signs:** Includes nuchal rigidity, headache, and photophobia.

15. Musculoskeletal: The musculoskeletal exam is typically tailored to the patient's concern

- Gross inspection
- Assess mobility (compare to unaffected side)
- Perform percussion and palpation (tenderness)
- Assessment of strength
- **Areas covered according to the patient concerns:** Back/spine, Shoulder, Elbow, Wrist, Hand, Knee and Hip

16. Breast

- **Inspection:** Skin changes (such as erythema, dimpling, scaling), nipple discharge
- **Palpation:** Breast masses, Breast tenderness.
- Performed while the patient is supine and with hands behind the head. Palpate in a concentric circle, verticle strip method, or "spokes of a wheel" method.
- **Axillary examination:** inspect and palpation of the axillary lymph nodes.

8. GIVE A DIFFERENTIAL DIAGNOSIS

- Considering and listing all possible explanations or causes for a patient's symptoms or condition.
- It helps healthcare providers narrow down the potential diagnoses through evaluation and testing to determine the most likely cause.

**9. TARGETED DIAGNOSTIC TESTING:**

The process of conducting relevant diagnostic tests and investigations to thoroughly evaluate a patient's medical condition and guide treatment decisions. This typically involves a systematic approach to gathering information through laboratory tests, imaging studies, and other diagnostic procedures.

➤ LABORATORY INVESTIGATIONS

1. **Complete Blood Count (CBC):** Assesses RBCs and WBCs, Hb levels, and platelet count.
2. **Comprehensive Metabolic Panel (CMP):** Evaluates kidney function and liver function, electrolyte levels, and blood glucose.
3. **Lipid Panel:** Cholesterol levels, including LDL, HDL, and triglycerides, to assess CVS risk.
4. **Liver Function Tests (LFTs):** Assesses liver health.
5. **Serum Electrolytes:** Assesses levels of sodium, potassium, chloride, & bicarbonate in the blood.
6. **Serum Creatinine:** Measures kidney function by assessing levels of creatinine in the blood.
7. **Coagulation Studies:** Evaluates blood clotting ability using tests such as PT (Prothrombin Time) and INR (International Normalized Ratio).
8. **Serum Uric Acid:** Measures uric acid levels in the blood to diagnose gout.
9. **Stool Occult Blood Test:** Detects hidden blood in stool to screen for colon CA & GI bleeding.
10. **Thyroid Function Tests (TFTs):** Measures TSH, T3 and T4 to rule out thyroid dysfunction.
11. **Blood Glucose Test:** Measures blood sugar levels to screen for and monitor diabetes.
12. **Hemoglobin A1c (HbA1c):** Reflects average blood sugar levels over the past 2-3 months and is used to monitor long-term diabetes control.
13. **Troponin Test:** Detects cardiac muscle damage, aiding in diagnosing myocardial infarction.
14. **Rheumatoid Factor (Rh Factor):** Detects antibodies associated with rheumatoid arthritis.
15. **CPK (Creatine Phosphokinase):** Measures levels of CPK, an enzyme released when muscle tissue is damaged, aiding in diagnosing muscle disorders like muscular dystrophy or myocardial infarction.
16. **Pulmonary Function Tests (PFTs):** Measures lung function, including airflow, lung volumes, and gas exchange, aiding in diagnosing conditions like asthma, chronic obstructive pulmonary disease (COPD), and restrictive lung diseases.
17. **STI Screening:** Testing for sexually transmitted infections (STIs) such as HIV, syphilis, gonorrhea, and chlamydia.
18. **Hormone Levels:** Measuring hormone levels (e.g., testosterone, FSH, LH, estrogen) to assess for hormonal imbalances.
19. **Urinalysis:** Detects urinary tract infections, kidney disorders, and other metabolic problems.
20. **Semen Analysis:** Evaluates sperm quantity and quality for male fertility.
21. **CSF Analysis:** Examines cerebrospinal fluid for diagnosing central nervous system conditions.
22. **Ascitic Fluid Analysis:** Assesses fluid in the abdomen to diagnose underlying causes of ascites.
23. **Sputum AFB Smear:** Detects Mycobacterium tuberculosis in sputum for tuberculosis diagnosis.
24. **Culture test:** To identify microorganisms from a sample of blood, urine, sputum, or pus.
25. **Pap smear:** Test used to screen for cervical cancer in women.
26. **PCR (NAAT):** To detect the presence of genetic material (RNA or DNA) from pathogens such as viruses or bacteria in patient samples. These tests are primarily used for diagnosing infectious diseases, including viral infections like influenza VIRUS, COVID-19, HIV, HCV, HBV, HSV, VZV, EBV & CMV. Bacterial infections, and sexually transmitted infections (STIs).

RADIOLOGICAL TESTS:

1. X-ray:

- **Chest X-ray:** Evaluates lung and heart conditions.
- **Abdominal X-ray:** Assesses abdominal organs.
- **Skeletal X-ray:** Images bones and joints.
- **Kidney x-ray:** Evaluates kidneys and bladder.

2. Ultrasound:

- **Abdominal Ultrasound:** Images abdominal organs.
- **KUB ultrasound:** Images of kidney urinary bladder
- **Pelvic Ultrasound:** images of pelvic organs like the uterus and ovaries
- **Prostate Ultrasound:** Evaluation of the prostate gland for abnormalities.
- **Testis Ultrasound:** Imaging of the testicle's condition e.g. tumors or infections.
- **Trans rectal ultrasound:** Rectal probe used to examine the prostate gland.
- **Transvaginal ultrasound:** Probe inserted into the vagina to see female reproductive organs.
- **Duplex ultrasound:** Doppler ultrasound to assess blood flow in vessels.
- **Thyroid Ultrasound:** Assesses thyroid gland.

3. CT scan (Computed Tomography):

- **CT head:** Images brain and skull.
- **CT chest:** Assesses lung and mediastinum.
- **CT Abdomen and Pelvis:** Evaluates abdominal and pelvic structures.
- **CT kidney:** Evaluates kidneys, ureter, and urinary bladder.
- **CT bone and joint**

4. MRI (Magnetic Resonance Imaging):

- **MRI Brain:** Evaluates brain structures.
- **MRI Spine:** Images spinal cord and vertebrae.
- **MRI Knee:** Assesses knee joint and surrounding structures.

5. Other radiological investigation:

- **Mammogram:** Screens for breast cancer in women.
- **DEXA Scan (Dual-Energy X-ray Absorptiometry):** Measures bone density, assessing osteoporosis risk and bone health.
- **Barium Swallow:** Visualizes upper gastrointestinal tract.
- **Intravenous Pyelogram (IVP):** Images urinary tract with contrast dye.
- **Arteriogram:** Evaluates blood vessels with contrast dye.
- **PET-CT (Positron Emission Tomography-Computed Tomography):** Detects cancerous tumors and assesses metabolic activity.

INVASIVE MEDICAL PROCEDURES:

This procedure involves inserting a flexible tube with a camera (endoscope) into the body to examine internal organs or cavities.

Examples include:

- **Colonoscopy:** Examining the colon.
- **Gastrosocopy:** Examining the stomach and upper gastrointestinal tract.
- **Bronchoscopy:** Examining the airways and lungs.
- **Cystoscopy:** Examining the bladder and urinary tract.
- **Laparoscopy:** Examining the abdominal organs.
- **Hysteroscopy:** Examining the uterus.
- **Cardiac catheterization:** involves inserting a thin tube into the heart through a blood vessel to diagnose or treat heart conditions.

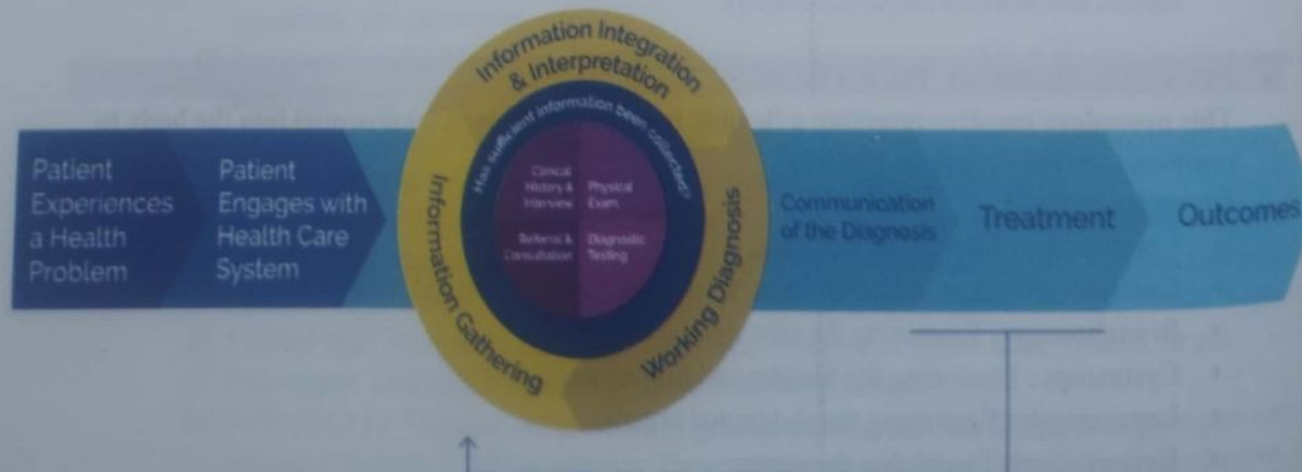


10. PROVISIONAL DIAGNOSE

-  ➤ **Patient History:** Mrs. Khan, a 65-year-old female, presents to the emergency department with complaints of worsening cough, fever, and shortness of breath for the past 5 days. She reports productive cough with yellowish sputum, fever with chills, and chest pain that worsens during deep breathing. She denies recent travel or sick contacts but mentions a history of hypertension.
- **Physical Examination:** Upon examination, Mrs. Khan appears ill and fatigued. Vital signs reveal a temperature of 102°F (38.9°C), heart rate of 100 beats per minute, respiratory rate of 24 breaths per minute, and oxygen saturation of 92% on room air. Auscultation of the lungs reveals coarse crackles in the right lower lung field. Percussion over the right lower lung field elicits dullness.
- **Diagnostic Workup:**
- **Chest X-ray:** Demonstrates consolidation in the right lower lobe with air bronchograms, suggestive of lobar pneumonia.
 - **Complete blood count (CBC):** Elevated WBCs with accounts shift.
 - **Sputum culture:** Positive for *Streptococcus pneumoniae*.
- **Provisional diagnosis:** Community-acquired pneumonia (CAP) due to *Strep. pneumoniae* infection.

11. MANAGEMENT PLAN

- Initiate empirical antibiotic therapy with oral levofloxacin 500mg x once daily for 5-7 days.
- Provide supportive treatment: Encourage oral fluid & nutritional support, analgesia for fever and pain, cough suppressants for excessive coughing.
- Administer supplemental oxygen to maintain SpO₂ > 90%.
- Encourage deep breathing exercises and chest physiotherapy to prevent atelectasis.
- Continuous monitoring of vital signs closely for clinical response.
- Consider hospital admission if there's worsening respiratory distress or sepsis.
- Provide patient education on the importance of completing the antibiotic course, recognizing complications, and follow-up appointments.
- **Follow-up:** Arrange follow-up appointment in one week to assess clinical improvement, repeat chest X-ray if necessary, and adjust management accordingly.



MOST OF THE PATIENTS COMING TO THE EMERGENCY OR OUTPATIENT DEPARTMENT HAVE THE FOLLOWING SYMPTOMS:



» Fever	» Cough	» Hematuria	» Headache
» Pain	» Sputum	» Vomiting	» Weakness
» Dyspnea	» Hemoptysis	» Diarrhea	» Mass
» Palpitations	» Haematochezia	» Seizures	»

1. FEVER

- **Onset:** "When did you first notice the fever, and did it come on suddenly or gradually?"
- **Duration:** "How long have you been experiencing fever, and does it come and go, or is it constant?"
- **Progression:** "Have you noticed any changes in the severity or frequency of your fever over time, or has it stayed the same?"
- **Aggravating factors:** "Do you notice anything that seems to make your fever worse, like physical activity, exposure to heat, or certain medications?"
- **Relieving factors:** "Is there anything that helps to reduce your fever, such as rest, drinking fluids, or taking medications?"
- **Associated symptoms:** "In addition to fever, do you have any other symptoms like chills, sweating, headache, body aches, cough, sore throat, nausea, vomiting, diarrhea, or rash? And can you describe any recent sick contacts or travel history?"

2. PAIN

- **Onset:** "When did you first notice the pain, and did it come on suddenly or gradually?"
- **Duration:** "How long have you been experiencing the pain, and does it come and go, or is it constant?"
- **Progression:** "Have you noticed any changes in the severity or frequency of your pain over time, or has it stayed the same?"
- **Aggravating factors:** "Do you notice anything that seems to make your pain worse, like movement, certain positions, or specific activities?"
- **Relieving factors:** "Is there anything that helps to alleviate your pain, such as rest, heat or cold therapy, medications, or changes in position?"
- **Associated symptoms:** "In addition to pain, do you have any other symptoms like nausea, vomiting, fever, or any changes in bowel or bladder habits? And can you describe the pain in terms of its location, quality, radiation, timing, and any factors that worsen or improve it?"

3. DYSPNOEA (BREATHLESSNESS)

- **Onset:** "When did you first notice the shortness of breath, and did it come on suddenly or gradually?"
- **Duration:** "How long have you been experiencing shortness of breath, and does it happen all the time or only sometimes?"
- **Progression:** "Have you noticed any changes in the severity or frequency of your shortness of breath over time, or has it stayed the same?"
- **Aggravating factors:** "Do you notice anything that seems to make your shortness of breath worse, like physical activity, lying flat, or exposure to certain environments?"
- **Relieving factors:** "Is there anything that helps to alleviate your shortness of breath, such as resting, sitting upright, or using medications?"
- **Associated symptoms:** "In addition to shortness of breath, do you have any other symptoms like cough, wheezing, chest pain, swelling in your ankles, or recent illness? And can you describe any previous lung conditions or respiratory infections?"

4. PALPITATION

- 
- **Onset:** "When did you first notice the palpitations, and did they come on suddenly or gradually?"
 - **Duration:** "How long have you been experiencing these palpitations, and do they come and go, or are they constant?"
 - **Progression:** "Have you noticed any changes in the severity or frequency of your palpitations over time, or have they stayed the same?"
 - **Aggravating factors:** "Do you notice anything that seems to make your palpitations worse, like certain activities, foods, or emotions?"
 - **Relieving factors:** "Is there anything that helps to alleviate your palpitations, such as relaxation techniques, avoiding triggers, or specific medications?"
 - **Associated symptoms:** "In addition to palpitations, do you have any other symptoms like chest pain, shortness of breath, dizziness, lightheadedness, fainting, sweating, or changes in heart rate or rhythm?"

5. COUGH

- **Onset:** "When did your cough start, and did it come on suddenly or gradually?"
- **Duration:** "How long have you been coughing, and does it come and go, or is it constant?"
- **Progression:** "Have you noticed any changes in your cough over time, such as it getting worse or better?"
- **Aggravating factors:** "Do you notice anything that seems to make your cough worse, like exposure to smoke, dust, or certain activities?"
- **Relieving factors:** "Is there anything that helps to relieve your cough, such as medications, drinking fluids, or using cough drops?"
- **Associated symptoms:** "In addition to the cough, do you have any other symptoms like presence of mucus (color, amount), chest pain, difficulty breathing, fever, or recent illness?"

6. SPUTUM

- **Onset:** "When did you start noticing sputum production, and did it happen suddenly or gradually?"
- **Duration:** "How long have you been producing sputum, and does it happen all the time or only sometimes?"
- **Progression:** "Have you noticed any changes in the amount or consistency of your sputum over time, or has it stayed the same?"
- **Aggravating factors:** "Do you notice anything that seems to make your sputum worse, like exposure to smoke, pollution, or certain activities?"
- **Relieving factors:** "Is there anything that helps to reduce or alleviate your sputum production, such as medications, drinking fluids, or using inhalers?"
- **Associated symptoms:** "In addition to sputum production, do you have any other symptoms like chest pain, cough, difficulty breathing, or fever? And can you describe the characteristics of your sputum, such as its color, consistency, or odor?"

7. HEMOPTYSIS

- **Onset:** "When did you first notice the coughing up of blood, and did it happen suddenly or gradually?"
- **Duration:** "How long have you been experiencing hemoptysis, and does it happen all the time or only sometimes?"
- **Progression:** "Have you noticed any changes in the amount or frequency of your hemoptysis over time, or has it stayed the same?"
- **Aggravating factors:** "Do you notice anything that seems to make your hemoptysis worse, like coughing, physical activity, or certain positions?"
- **Relieving factors:** "Is there anything that helps to reduce your hemoptysis, such as resting, avoiding respiratory irritants, or taking medications?"
- **Associated symptoms:** "In addition to coughing up blood, do you have any other symptoms like chest pain, shortness of breath, fever, weight loss, or night sweats? And can you describe your cough in terms of its presence, frequency, and character?"



8. HAEMATOCHEDIA

- **Onset:** "When did you first notice the passage of fresh blood through the anus, and did it happen suddenly or gradually?"
- **Duration:** "How long have you been experiencing haematochezia, and does it happen all the time or only sometimes?"
- **Progression:** "Have you noticed any changes in the severity or frequency of haematochezia over time, or has it stayed the same?"
- **Aggravating factors:** "Do you notice anything that seems to make your haematochezia worse, like certain foods or bowel movements?"
- **Relieving factors:** "Is there anything that helps to alleviate your haematochezia, such as dietary changes, medications, or treatments?"
- **Associated symptoms:** "In addition to passing fresh blood through the anus, do you have any other symptoms like abdominal pain, changes in bowel habits, constipation, diarrhea, weight loss, or other gastrointestinal symptoms?"

9. HAEMATURIA

- **Onset:** "When did you first notice blood in your urine, and did it happen suddenly or gradually?"
- **Duration:** "How long have you been experiencing haematuria, and does it happen all the time or only sometimes?"
- **Progression:** "Have you noticed any changes in the severity or frequency of haematuria over time, or has it stayed the same?"
- **Aggravating factors:** "Do you notice anything that seems to make your haematuria worse, like physical activity, certain foods or drinks, or medications?"
- **Relieving factors:** "Is there anything that helps to alleviate your haematuria, such as drinking more fluids, avoiding certain foods or drinks, or taking medications?"
- **Associated symptoms:** "In addition to blood in your urine, do you have any other symptoms like pain or discomfort during urination, urgency, frequency of urination, lower abdominal pain, back pain, fever, or any recent history of trauma or injury to your urinary tract?"

10. VOMITING

- **Onset:** "When did your vomiting start? Has it been happening for a while, or did it come on suddenly?"
- **Duration:** "How often are you vomiting, and how long has this been going on?"
- **Progression:** "Have you noticed if the vomiting is getting better, worse, or staying the same?"
- **Aggravating factors:** "Is your vomiting forceful or projectile? Have you experienced any symptoms like neck stiffness or sensitivity to light?"
- **Relieving factors:** "Does eating or drinking anything make your vomiting better or worse? Do you find that certain times of day are worse for vomiting?"
- **Associated symptoms:** "Can you describe the vomit for me? What does it look like? Is there any blood in it? Do you have any pain in your upper abdomen or anywhere else?"

11. DIARRHEA

- **Onset:** "When did your diarrhea start? Did it come on suddenly, or has it been developing over time?"
- **Duration:** "How long have you been experiencing diarrhea, and has it been continuous or coming and going?"
- **Progression:** "Have you noticed if the diarrhea is getting better, worse, or staying about the same?"
- **Aggravating factors:** "Have you noticed any specific foods or activities that seem to make your diarrhea worse?"
- **Relieving factors:** "Is there anything that helps to relieve your diarrhea, such as certain foods or over-the-counter medications?"
- **Associated symptoms:** "In addition to diarrhea, have you been experiencing any other symptoms like abdominal pain, cramping, bloating, fever, or noticing blood in your stool?"

12. SEIZURES

- 
- **Onset:** "When did you have your first seizure, and can you describe what happened?"
 - **Duration:** "How long do your seizures typically last, and do they vary in duration?"
 - **Progression:** "Have you noticed any changes in your seizures over time, such as becoming more frequent or severe?"
 - **Aggravating factors:** "Do you notice anything that seems to trigger your seizures, like stress, lack of sleep, or certain activities?"
 - **Relieving factors:** "Is there anything that helps to prevent or reduce the severity of your seizures, such as taking medications or avoiding triggers?"
 - **Associated symptoms:** "Besides the seizure itself, do you experience any warning signs before a seizure, or any other symptoms like muscle stiffness, confusion, or tiredness afterward?"

13. HEADACHE

- **Onset:** "When did you first notice the headache, and did it come on suddenly or gradually?"
- **Duration:** "How long have you been experiencing the headache, and does it come and go, or is it constant?"
- **Progression:** "Have you noticed any changes in the severity or frequency of your headache over time, or has it stayed the same?"
- **Aggravating factors:** "Do you notice anything that seems to make your headache worse, like stress, certain foods or drinks, lack of sleep, or exposure to noise or bright lights?"
- **Relieving factors:** "Is there anything that helps to alleviate your headache, such as rest, hydration, over-the-counter pain medications, or specific treatments prescribed by your doctor?"
- **Associated symptoms:** "In addition to the headache, do you have any other symptoms like nausea, vomiting, sensitivity to light or sound, changes in vision, neck stiffness, or recent head trauma?"
- **Character:** "Can you describe the quality or nature of the pain? Is it sharp, dull, throbbing, or pulsating?"

14. WEAKNESS

- **Onset:** "When did you first notice the weakness, and did it happen suddenly or gradually?"
- **Duration:** "How long have you been experiencing weakness, and does it come and go, or is it constant?"
- **Progression:** "Have you noticed any changes in the severity or frequency of your weakness over time, or has it stayed the same?"
- **Aggravating factors:** "Do you notice anything that seems to make your weakness worse, like certain activities or movements?"
- **Relieving factors:** "Is there anything that helps to alleviate your weakness, such as rest, specific exercises, or medications?"
- **Associated symptoms:** "In addition to weakness, do you have any other symptoms like fatigue, numbness or tingling, difficulty walking or moving, changes in sensation, or any recent illness or injury?"

15. MASS

- ☞ **Site and Characteristics:** Identify location, size, shape, and count (single or multiple).
- ☞ **Surface and Edge:** Note texture (smooth, rough, or indurated) and edge definition.
- ☞ **Consistency:** Assess if it's soft, spongy, or firm.
- ☞ **Mobility and Attachment:** Test mobility in two directions, note attachment.
- ☞ **Tenderness:** Ask about pain, check for nerve involvement.
- ☞ **Pulsation:** Feel pulsation with two fingers method.
- ☞ **Fluctuation:** Tap the center to check for fluctuation.
- ☞ **Irreducible:** Determine if it's compressible or reducible.

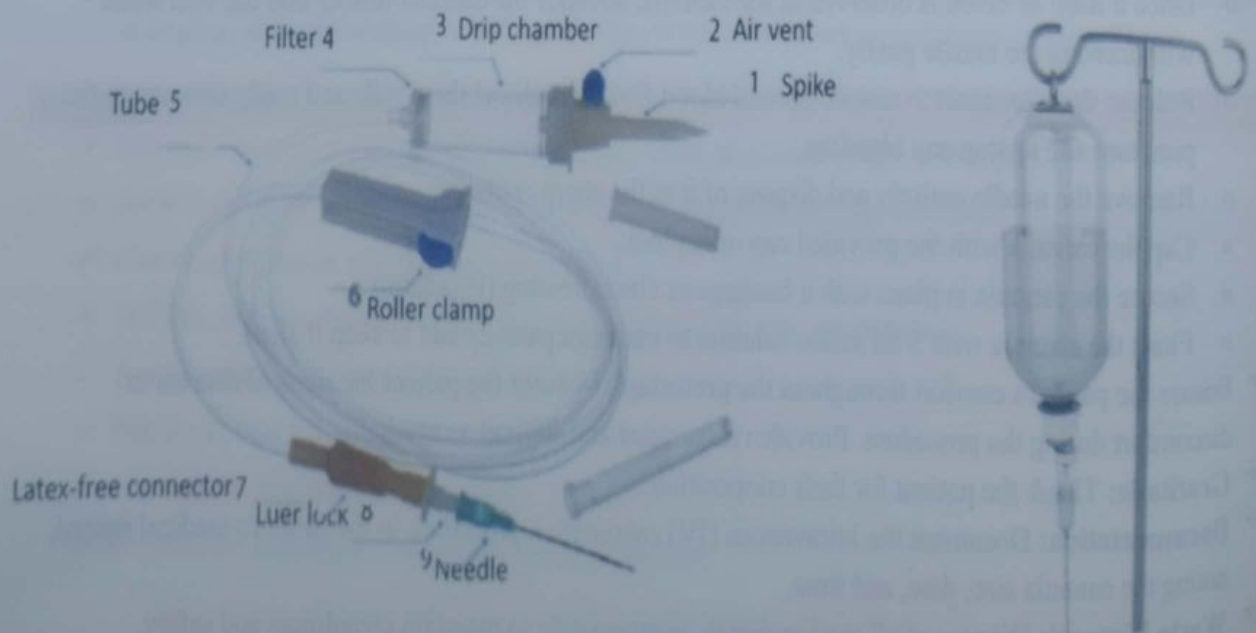
PASSING INTRAVENOUS LINE (IV CANNULATION)

- ☞ Introducing yourself to the patient and confirming their name and age for identification.
- ☞ Begin by providing a clear explanation of the **procedure and obtaining informed consent** from the patient. For example, "I will be inserting a thin plastic tube into one of the veins on your arm to administer intravenous (IV) fluids and medications. You may feel a sharp prick when the needle is inserted, but discomfort should subside once the tube is in place. Do you have any questions?"
- ☞ **Equipment collection:** Gather all necessary equipment required for the procedure in a clean try.
 1. A pair of non-sterile gloves, a tourniquet (a band to tie around the arm), Sterets alcohol wipes or pre-packaged cleaning sponges of chlorhexidine.
 2. An IV cannula of appropriate size. Size is primarily determined by the viscosity of the fluid to be infused (e.g. blood requires pink or larger) and the required rate of infusion.
 3. A pre-filled 5 ml syringe containing saline flush.
 4. An adhesive plaster/sticky bandage or clear dressing.
- ☞ **Hand Hygiene:** Thoroughly wash and dry your hands to maintain a sterile environment.
- ☞ Ask the patient to choose which arm they prefer for IV cannulation and to roll up their sleeve.
- ☞ Ensure the patient is comfortable and position their arm straight.
- ☞ **Tourniquet:** Apply a tourniquet a few inches above where you're going to put the needle.
- ☞ **Vein Palpation:** Palpate (feel) the arm to locate a suitable vein, preferably choosing one that is large and straight, avoiding the dorsum of the hand and the antecubital fossa if possible.
- ☞ **Intravenous Cannulation Procedure:**
 - » Perform hand hygiene and put on sterile gloves to prevent contamination during the procedure.
 - » Clean the skin using alcohol wipes or chlorhexidine sponges and allow it to dry.
 - » Remove the cannula from its packaging and take off the needle cap.
 - » Hold the skin taut and insert the cannula at an angle of approximately 30 degrees.
 - » Once a flash of blood is observed in the cannula, advance the cannula further into the vein while withdrawing the needle gently.
 - » Release the tourniquet to restore normal blood flow, withdrawl the needle and apply pressure to the puncture site to stop any bleeding.
 - » Remove the needle entirely and dispose of it in the sharp container.
 - » Cap the cannula with the provided cap or heplock.
 - » Secure the cannula in place with a bandage or clear dressing (tegaderm).
 - » Flush the cannula with 5 ml saline solution to maintain patency and to keep it clear.
- ☞ Ensure the patient's comfort throughout the procedure. Monitor the patient for signs of distress or discomfort during the procedure. Provide reassurance and support as needed.
- ☞ **Gratitude:** Thank the patient for their cooperation.
- ☞ **Documentation:** Document the intravenous (IV) cannulation procedure in the patient's medical record, noting the cannula size, date, and time.
- ☞ **Waste Disposal:** Dispose of all used materials appropriately to maintain cleanliness and safety.



SETTING UP AN INFUSION SET (A DRIP SET)

- ☞ Introducing yourself to the patient and confirming their name and age for identification.
- ☞ Provide a clear explanation of the procedure and obtain informed consent from the patient.
- ☞ **Gather the Equipment:** Gather all necessary equipment required for the procedure, including the infusion bag, infusion set, sterile gloves, antiseptic solution, and tape. Check the expiration date and integrity of the infusion bag and set.
- ☞ **Check Prescription and Fluid Bag:** Verify the fluid prescription on the chart (if applicable). Ensure the fluid bag contains the correct solution type and concentration and check its expiry date.
- ☞ **Prepare Fluid Bag:** Remove the IV fluid bag from its packaging and hang it on the drip stand.
- ☞ **Prepare Drip Set:** Remove the drip set from its packaging, ensuring the clamp is closed.
- ☞ **Prime the tubing:** Squeeze and release the collecting chamber of the drip set until it's half full. Then, open the clamp to let fluid flow and remove air bubbles. Finally, ensure fluid reaches the end of the tubing by opening its clamp.
- ☞ **Connect Extension Set (If Applicable):** If using an Octopus Extension set or connector, open it and clean it with saline to remove any air.
- ☞ **Connect Drip Set to Patient:** Instead of capping the cannula immediately after removing the needle, connect the drip set directly and flush it with fluid from the bag.
- ☞ **Secure Cannula and Tubing:** Apply a bandage or clear dressing (Tegaderm) over the cannula to secure it in place. Tape the tubing to the patient's arm to prevent dislodgement.
- ☞ **Adjust Drip Rate:** Set or adjust the drip rate according to the prescribed infusion rate (1 drop per second is approximately equal to 1 liter every 6 hours). Monitor Patient Comfort and Response:
- ☞ Ensure the patient's comfort throughout the procedure. Monitor the patient for signs of distress or discomfort during the procedure. Provide reassurance and support as needed.
- ☞ **Gratitude:** Thank the patient for their cooperation.
- ☞ **Documentation:** Document the procedure in the patient's medical chart, sign the fluid chart, and clearly note the date and time of the intervention.
- ☞ **Waste Disposal:** Dispose of all used materials appropriately to maintain cleanliness and safety.



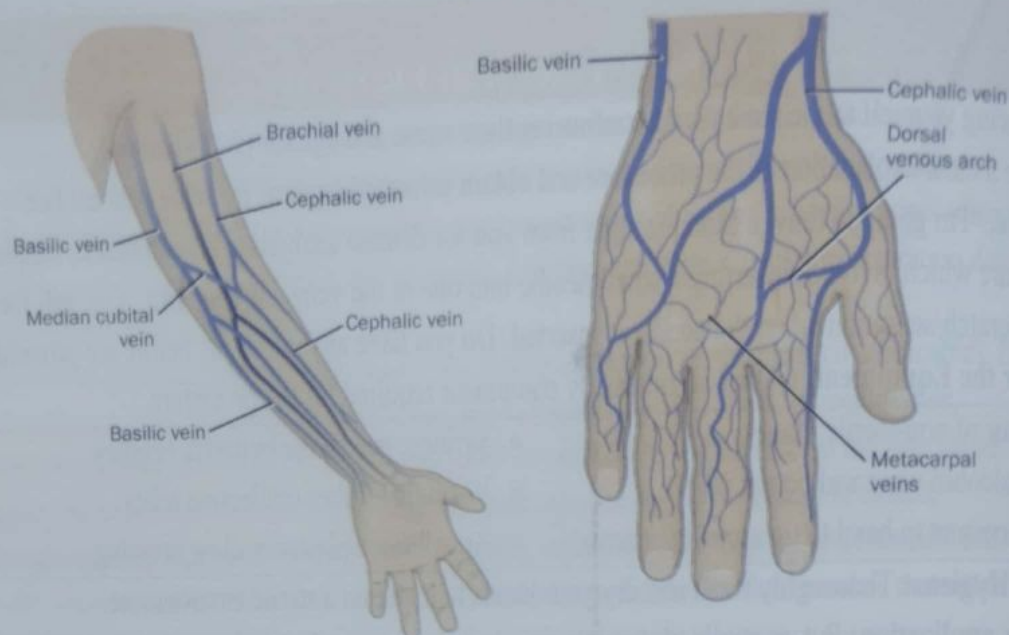
VENEPUNCTURE (PHLEBOTOMY)

- ☞ Introducing yourself to the patient and confirming their name and age for identification.
- ☞ Provide a clear explanation of the procedure and obtain informed consent from the patient. For example, "I'm going to draw a blood sample from you for disease analysis. This is a quick, simple procedure which involves inserting a small needle into one of the veins on your arm. You will feel a sharp scratch/sensation when the needle is inserted. Do you have any questions before we proceed?"
- ☞ **Gather the Equipment:** Gather all necessary equipment required for the procedure.



- | | |
|---|--|
| » A pair of non-sterile gloves | » Syringe, needles or butterfly needles. |
| » An alcohol wipe and cotton wool | » Vacutainer tubes (collection tube) |
| » Tourniquet (a band to tie around the arm) | » An adhesive plaster or clear dressing. |

- ☞ **Hand Hygiene:** Thoroughly wash and dry your hands to maintain a sterile environment.
- ☞ **Gloves application:** Put on sterile gloves to prevent contamination during the procedure.
- ☞ Ask the patient to choose which arm they prefer to have blood taken from and to roll up their sleeve.
- ☞ Ensure the patient is comfortable and position their arm straight.
- ☞ **Tourniquet:** Apply a tourniquet a few inches above where you're going to put the needle.
- ☞ **Vein Palpation:** Palpate (feel) the arm to locate a suitable vein, preferably choosing one that is large and straight, avoiding the dorsum of the hand and the antecubital fossa if possible. The vein selected is most commonly the median cubital vein in the antecubital fossa.
- ☞ **Blood collection (Venipuncture):**
 1. Perform hand hygiene and put on sterile gloves to prevent contamination during the procedure.
 2. Clean the skin using alcohol wipes or chlorhexidine sponges and allow it to dry.
 3. Choose an appropriate size needle or butterfly (usually 21–23 gauge) and connect it to a syringe or vacutainer system. Hold the skin taut below the puncture site, then insert the needle smoothly into the vein, aiming towards the center at a 15–30-degree angle.
 4. Once the blood is flowing well, follow the instructions from the manufacturer to fill the Vacutainer tube. Once all the necessary tubes are filled, release the tourniquet. Remember that the tubes need to be filled in a certain order (bottles with no additives first).
 5. Release the tourniquet to restore normal blood flow, withdraw the needle and apply pressure to the puncture site to stop any bleeding.
 6. Label each blood culture bottle with patient identification information, date, and time of collection.
 7. Fill in the blood request form (at least: patient's name, date of birth, and hospital number; date of blood collection; tests required).
- ☞ Ensure the patient's comfort throughout the procedure. Monitor the patient for signs of distress or discomfort during the procedure. Provide reassurance and support as needed.
- ☞ **Gratitude:** Thank the patient for their cooperation.
- ☞ **Documentation:** Document the procedure in the patient's medical record, including blood tests that have been requested in the patient's notes.
- ☞ **Waste Disposal:** Dispose of all used materials appropriately to maintain cleanliness and safety.



- ☞ Preferred site: antecubital fossa, where arms bend at the elbow
- ☞ Preferred vein for venepuncture: Median cubital vein.

N.B. The basilic vein (lies closely to the brachial nerve and artery), median cubital vein (preferred), and cephalic vein (tendency to roll) are superficial veins that are frequently selected for venipuncture at the cubital fossa because of its characteristics: a thick lumen and an easily visible confirmation.

If the veins are not apparent

- » Lower the arm over the bedside.
- » Ask the patient to exercise his arm by repeatedly clenching his fist.
- » Gently tap the venepuncture site with two fingers.
- » Apply a warm compress to the venepuncture site.
- » Do not cause undue pain to the patient by trying repeatedly (more than 2–3 times) call a more experienced colleague instead.
- » Use femoral stab only as a last resort (usually in CPR situations).

In the event of a needlestick injury

- » Encourage bleeding, wash with soap and running water.
- » Immediately report the injury to your supervisor or the occupational health service.
- » If there is a significant risk of HIV, post-exposure prophylaxis should be started as soon as possible.
- » Fill out an incident form.



VACUTAINER TUBE (COLLECTION CONTAINERS) CHART

Haemoguard Stopper	Tube content	Determination	
BLUE TOP TUBE 	SODIUM CITRATE	PT, aPTT, INR D-Dimers Fibrinogen Factor levels	FDPs Coagulation screen Thrombophilia screen Lupus Anticoagulant screen
PURPLE TOP TUBE 	ANTI COAGULANTS = EDTA	Whole blood & morphology, CBC, Blood smear, Reticulocyte count, HbA1C ESR, blood bank (crossmatch) Parathyroid hormone (PTH) Red cells level, folate level PCR genetic testing,	Direct comb test G6PD, Malaria Parasites Flowcytometry Monospot test (EBV) Hb electrophoresis Cord Blood Samples Blood bank procedures
GREEN TOP TUBE 	LITHIUM OR SODIUM HEPARIN	Metabolic test, Blood gas analysis, Ammonia Renin and aldosterone Insulin	Plasma preparation for some test FSH, LH
YELLOW TOP TUBE 	GEL TUBE - Serum separating tube (SST) No anticoagulant	LFTs - Direct and indirect bilirubin, ALT, AST, ALP, GGT, Total protein & albumin, TPAGR RFTs, BUN and creatinine Serum electrolytes CRP Serum magnesium Serum calcium Serum phosphate HIV Amylase and Lipase CPK Blood glucose (FBS/RBS) Uric acid Indirect coomb test Osmotic fragility test Toxicology Immunoglobulin Bone profile	Complement level: C3, C4 Auto-antibody screen: Thyroid antibodies, ANA, Hepatitis A & Hepatitis E antibodies, Rh factor, SLE antibodies testing. HCV testing, HBV testing Dengue NS1 Serum LDH Vitamin B12 Iron studies. Ferritin Lipid profile TFTs (T3, T4 & TSH) Cortisol Testosterone Calcitonin Growth hormone IGF-1, Insulin, C-peptide Beta HCG Troponin HLA testing
GREY TOP TUBE 	ANTICOAGULANTS SODIUM FLUORIDE	Glucose tolerance testing (maintain plasma glucose level) Lactate (lactic acids) Pyruvate testing	
RED TOP TUBE 	No additive (No anticoagulants)	Chemistry tests: glucose, electrolytes, liver enzymes Serological tests: HIV, syphilis, immunological test Drug levels, and blood bank procedures, FSH, LH	



Blood Tube Color Chart for specimens submitted to University of Colorado Hospital Laboratory

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GOLD or RED W/GEL-SERUM SEPARATOR (SST)

Test Name	Alt Spec	Add-on
Acute Hepatitis Panel	None	2d
Alpha Feto Protein	None	2d
ANA Screen	None	7d
B19 Parvovirus PCR	Lav EDTA	3d
Beta-2 Microglobulin	None	3d
C3	None	8d
C4	None	8d
CA125	None	2d
CA2729	None	5d
CEA	None	2d
Ceruloplasmin	None	3d
Celiac Panel	None	7d
CMV Antibody	None	2d
Cortisol	None	2d
Digoxin	None	2d
dsDNA	None	7d
EBV Antibody	None	2d
Estradiol	None	2d
FSH	None	2d
Haptoglobin	None	7d
HCG Qualitative	None	2d
Hep A Antibody	None	7d
Hep B Core IgM	None	2d
Hep B Core Antibody	None	3d
Hep B Surface Antibody	None	7d
Hep B Surface Antigen	None	7d
Hep C Antibody	None	7d
HIV 1-2 Abs Ag Screen	None	3d
HSV Antibody	None	7d
Immunofixation Electrophor	None	7d
Immunoglobulins	None	3d
Insulin	None	1d
Kappa Lambda Free	None	7d
Luteinizing Hormone (LH)	None	2d
Lithium	None	7d
Mumps IgG	None	9d
Osmolality	Li Hep	5d
PSA	None	1d
Rubella IgG	None	9d
Serum Protein Electrophor	None	7d
Syphilis	None	7d
Testosterone	None	7d
Toxoplasma gondii	None	7d
Thyroglobulin	None	2d
Thyroglobulin Antibody	None	2d
Vitamin D25	None	7d
Vancella zoster Antibody	None	7d

RED NO GEL

Test Name	Alt Spec	Add-on
Ethanol GC	None	7d
Glycols	None	1d
Isopropanol GC	None	7d
Keppra	None	7d
Lamotrigine	None	7d
Lidocaine	None	5d
Methanol GC	None	7d
Mixed Alcohols	None	7d
Pentobarbital	None	7d
Phenytoin free & total	None	7d
Progesterone	None	2d

Alt Spec = Alternative Specimen Container

Add-on = Add-on Stability in days (d) or hours (hrs)

+ = Submit specimens on ice

= Protect specimens from light

Questions? Contact University of Colorado Hospital Clinical Laboratory at 720.848.4401 or visit our Lab Test Catalog in the Source for complete testing information and the most recent version of this chart.

GREEN WITH GEL - LITHIUM HEPARIN (LiHep)

Test Name	Alt Spec	Add-on
Basic Metabolic Panel	None	3d
Complete Metabolic Panel	None	3d
Electrolyte Panel	None	1d
Hepatic Function Panel	None	3d
Lipid Panel	None	7d
Renal Function Panel	None	3d
Acetaminophen	None	1d
Albumin	None	7d
Alkaline Phosphatase (ALP)	None	4d
ALT	None	3d
Amylase	None	7d
AST	None	7d
B12	SST	2d
Beta-HCG	SST	2d
BHB	None	7d
Bilirubin Direct #	None	3d
Bilirubin Total #	None	7d
BUN	None	7d
CA19-9	None	2d
Calcium	None	7d
Carbamazepine	None	7d
Carbon Dioxide	None	1d
CK	None	12h
CKMB	None	2d
Chloride	None	7d
Cholesterol	None	7d
Creatinine	None	7d
CRP/hsCRP	None	7d
C-Peptide	SST	2d
Ethanol	None	3d
Ferritin	None	2d
Folate #	SST	8hrs
Free T4	None	2d
GGT	None	3d
Gentamicin	None	2d
Glucose	None	3d
HDL	None	5d
Iron Binding Panel	None	2d
LDH	None	2d
Lipase	SST	5d
Magnesium	None	7d
Phenobarbital	None	7d
Phosphorus	None	7d
Potassium	None	7d
Prealbumin	None	7d
Procalcitonin	SST	2d
Protein total	None	7d
PTH	SST	2d
Salicylate	N/A	1d
Sodium	None	7d
Theophylline	None	7d
Tobramycin	None	2d
Transferin	None	7d
Triglycerides	None	7d
Troponin	None	1d
TSH	SST	7d
Uric Acid	None	5d
Valproic acid	None	7d
Vancomycin	None	8hrs
Vitamin B12	SST	2d

GREEN NO GEL - LITHIUM HEPARIN (LiHep)

Test Name	Alt Spec	Add-on
Carboxyhemoglobin	NaHep	0.5hr
Electrolytes, Whole Blood	None	0.5hr
Glucose, Whole Blood	NaHep	0.5hr
Ionized Calcium	NaHep	0.5hr
Methemoglobin	NaHep	0.5hr
Lactate, Whole Blood	NaHep	0.5hr
Potassium, Whole Blood	NaHep	0.5hr
Sodium, Whole Blood	None	0.5hr

LAVENDER - EDTA (Lav EDTA)

Test Name	Alt Spec	Add-on
CBC	None	7d
Blood parasites	None	N/A
CD34	None	1d
Cyclosporine	None	7d
ESR	None	7d
Fetal Hemoglobin	None	8hrs
Hematocrit	None	2d
Hemoglobin	None	2d
Hemoglobin A1c	None	7d
Hemoglobin Electrophoresis	None	7d
Homocysteine +	None	N/A
Plasma Hemoglobin	None	7d
Platelet Count	None	2d
Reticulocyte count	None	2d
Siroimus	None	7d
Tacrolimus	None	3d

LIGHT BLUE - SODIUM CITRATE

Test Name	Alt Spec	Add-on
Antithrombin Activity	None	8hrs
APC Resistance	None	4hrs
D-Dimer	None	8hrs
Dilute Thrombin Time	None	8hrs
Fibrinogen	None	8hrs
Euglobulin Lysis Time	None	4hrs
Heparin level	None	2hrs
HIT	None	1hr*
Lupus Anticoagulant Panel	None	4hrs
PTT	None	4hrs
Protein C Activity	None	8hrs
Protein S Free Antigen	None	1hr*
PT	None	8hrs*
Rotem	None	4hrs
RVVT	None	4hrs
Silica Clotting Time	None	4hrs
Specific Factor Activity	None	4hrs
Specific Factor Inhibitor	None	4hrs
TEG	None	2hrs
Thrombin Time	None	8hrs
Von Willebrand Panel	None	4hrs

*Stability periods are for samples at ambient temp.

PINK - EDTA

Test Name	Alt Spec	Add-on
Blood Bank	None	3d
Adenovirus PCR, Plasma	Lav EDTA	3d
Ammonia +	None	3hrs
BK Virus PCR, Plasma	Lav EDTA	3d
BNP	Lav EDTA	3d
Cytomegalovirus PCR	Lav EDTA	3d
Enterovirus PCR, Plasma	Lav EDTA	2d
EBV PCR	Lav EDTA	3d
HSV PCR	Lav EDTA	3d
HHV6 PCR	Lav EDTA	3d
HHV8 PCR	Lav EDTA	3d
HBV, HCV, HIV by PCR	Lav EDTA	6d

GREEN NO GEL - SODIUM HEPARIN (NaHep)

Test Name	Alt Spec	Add-on
Blood Culture - Quantitative	None	None
Pour Plate (submit along with blood culture bottles)	None	None
Flow Cytometry:		
IFL	Lav EDTA	3d
CD3/CD4 count	None	24hrs
CD30 Panel, Pre Car T-Cell	None	24hrs
T-Cell B-Cell Panel	None	24hrs
TBANK, Transplant CD3	None	24hrs

BLOOD CULTURES

- ☞ Introducing yourself to the patient and confirming their name and age for identification.
- ☞ Provide a clear explanation of the procedure and obtain informed consent from the patient.
For example, "I'm going to take a small sample of your blood for testing. I will use a small, tiny needle to draw blood from a vein in your arm. You will feel a sharp pinch/scratch when I insert the needle. Is there anything you'd like to ask before we start?"

- ☞ **Gather the Equipment:** Gather all necessary equipment required for the procedure.

» A pair of non-sterile gloves	» Needles, butterfly needles, or Syringe.
» An alcohol wipe and cotton wool	» Blood culture bottles x 2 (anaerobic and aerobic)
» Tourniquet	» An adhesive plaster or clear dressing.

- ☞ **Hand Hygiene:** Thoroughly wash and dry your hands to maintain a sterile environment.
- ☞ **Gloves application:** Put on sterile gloves to prevent contamination during the procedure.
- ☞ Ask the patient to choose which arm they prefer to have blood taken from and to roll up their sleeve.
- ☞ Ensure the patient is comfortable and position their arm straight.
- ☞ **Tourniquet:** Apply a tourniquet (a band) a few inches above where you're going to put the needle.
- ☞ **Vein Palpation:** Palpate (feel) the arm to locate a suitable vein, preferably choosing one that is large and straight, avoiding the dorsum of the hand and the antecubital fossa if possible. The vein selected is most commonly the median cubital vein in the antecubital fossa.
- ☞ For the blood culture bottles, check types (aerobic and anaerobic) and expiry dates, and ensure that the broth is clear. Do not remove the barcodes.
- ☞ **Perform hand hygiene and put on sterile gloves.**
- ☞ Clean the skin using alcohol wipes using circular motion and allow it to dry.
- ☞ Remove the flip tops from the culture bottles and disinfect the rubber caps with a fresh alcohol swab.
- ☞ **Blood collection (Venipuncture):**
 8. Perform hand hygiene and put on sterile gloves to prevent contamination during the procedure.
 9. Choose an appropriate size needle or butterfly (usually 21–23 gauge) and connect it to a syringe or vacutainer system. Hold the skin taut below the puncture site, then insert the needle smoothly into the vein, aiming towards the center at a 15–30-degree angle.
 10. Once the blood is flowing well, follow the instructions from the manufacturer to fill the blood culture bottles. Each bottle needs a specific volume of blood to be drawn, usually around 10 ml. Start by filling the aerobic bottle, then the anaerobic one to keep air out. If you're using a needle and syringe, draw at least 20 ml of blood to make sure you have enough for each bottle. Try not to change needles to keep things clean and safe.
 11. Release the tourniquet to restore normal blood flow, withdraw the needle and apply pressure to the puncture site to stop any bleeding.
 12. Label each blood culture bottle with patient identification information, date, and time of collection.
 13. Convey the samples to the microbiology laboratory without delay (or else incubate the bottles).
- ☞ Ensure the patient's comfort throughout the procedure. Monitor the patient for signs of distress or discomfort during the procedure. Provide reassurance and support as needed.
- ☞ **Gratitude:** Thank the patient for their cooperation.
- ☞ **Documentation:** Document the procedure in the patient's medical record, including the number and type of blood culture bottles collected.
- ☞ **Waste Disposal:** Dispose of all used materials appropriately to maintain cleanliness and safety.



BLOOD TRANSFUSION

1. Introduce yourself to the patient and confirm the name and age of the patient.
2. Introducing yourself to the patient and confirming their name and age for identification.
3. Provide a clear explanation for the requirement of a blood transfusion, explain the complications, and obtain informed consent from the patient.
4. **Monitor and record VITAL SIGNS:** Pulse, Blood pressure, Respiration, temperature and SpO₂.

1) SAMPLE COLLECTION

- » Re-confirm the patient's name and age and check his identity bracelet.
- » Extract 3 – 5ml (Maximum 10 ml) of blood for blood grouping and cross match
- » Label the tube and request form with the patient's identifying data: name, age, and hospital number.
- » Fill out a blood transfusion form, specifying the total number of units required.
- » Ensure that the tube reaches the laboratory promptly.

2) BLOOD TRANSFUSION PRESCRIPTION

- » Prescribe the number of units of blood required in the intravenous infusion section of the patient's prescription chart. Each unit of blood should be prescribed separately and be administered over a period of 4 hours.
- » If the patient is elderly or has a history of heart failure, consider prescribing furosemide (loop diuretic) with the second and fourth units of blood.
- » Arrange for the blood bag to be delivered. The blood transfusion must start within 30 minutes of the blood leaving the blood refrigerator.

3) CHECKING PROCEDURES

- » **Ask a registered RN or another doctor (HO/PGI) to go through below checking procedures with you:**
 - A. Positively identify the patient by asking him for his name, Age, and address.
 - B. Confirm the patient's identifying data and ensure that they match those on his identity bracelet, case notes, prescription chart, and blood compatibility report.
 - C. Record the blood group and serial number on the unit of blood and make sure that they match the blood group and serial number on the blood compatibility report and the blood compatibility label attached to the blood unit.
 - D. Date and time of blood Transfusion.
 - E. Check the expiry date on the unit of blood.
 - F. Inspect the blood bag for leaks or blood clots or discoloration.

4) BLOOD ADMINISTRATION

- » Attach one end of the transfusion giving set to the blood bag and run it through to ensure that any air in the tubing has been expelled. Note that a transfusion giving set has an integral filter and is not the same as a standard fluid giving set.
- » Attach the other end of the giving set to the IV cannula which should be a grey (16G), wide-bore cannula (minimum pink/20G, or larger for resuscitation situations).
- » Adjust the drip rate so that the unit of blood is administered over 4 hours. Because one unit of blood is 300 ml, and because 15 drops are equivalent to about 1 ml, this amounts to about 19 drops/minute.
- » Sign the prescription chart and blood compatibility report, noting the start time of transfusion. Ensure both documents are also signed by a checking colleague.

5) PATIENT MONITORING & COMFORT

- » **Monitor and record the patient's vital signs:** Pulse rate, blood pressure, temperature and SpO₂ at 0, 15, and 30 minutes, and then hourly thereafter.
- » Ensure the patient's comfort throughout the procedure. Monitor the patient for signs of anaphylaxis – adverse transfusion reactions such as fever, tachycardia, hypotension, urticaria, nausea, chest pain, and breathlessness. Provide reassurance and support as needed.
- » **Gratitude:** Thank the patient for their cooperation
- » **Documented the procedure** in the patient's medical record, including anaphylaxis– adverse transfusion reactions such as fever, tachycardia, hypotension, urticaria, nausea, chest pain, and breathlessness.

GUIDELINES FOR BLOOD TRANSFUSION

1. WHOLE BLOOD (WB) / PACKED RED CELL (PCV)

- **Volume:**
 - **WB:** Around 450 mL per unit.
 - **PCV:** Contains concentrated red blood cells, usually around 200-300 mL per unit.
- **Content:**
 - **WB:** Contains RBCs, WBCs, platelets, plasma, and various proteins and nutrients.
 - **PCV:** Primarily consists of RBCs, with minimal plasma and other components.
- **Storage:** both typically stored in refrigerators at temperatures between 1°C – 6°C.
- **Shelf life:**
 - **WB:** Typically has a shelf life of around 35 – 42 days when stored properly.
 - **PCV:** Shelf life is typically shorter than WB, usually around 35 days.
- **Indication:**
 - » **Whole blood:** RBCs replacement with hypovolemia
 - Primarily used in cases of acute blood loss or when multiple blood components are required.
 - Elective autologous blood transfusion for elective surgery
 - » **PCV:** RBCs replacement in severe anemia or to increase oxygen-carrying capacity.
 - 1) To maintain organ perfusion or to increase oxygen-carrying capacity.
 - 2) Hospitalized patients (independent of clinical findings) $Hb \leq 6$ g/dL
 - 3) Hospitalized patients (hemodynamically stable) $Hb < 6 - 7$ g/dL
 - 4) Acute hemorrhage and/or hypovolemic shock (e.g., gastrointestinal bleeding, trauma)
 - 5) Symptomatic anemia (e.g., G6PD deficiency, aplastic anemia, β -thalassemia, sickle cell disease, anemia of chronic kidney disease)
- **Special instruction:**
 - » **Compatibility Check:** Ensure ABO and Rh compatibility with recipient, and cross matching.
 - » **Transfusion Time Limit:** Complete transfusion within 4 hours (for WB) or 3 hours (for PCV).
 - » **Medication Caution:** Do not add medication to the blood unit during transfusion.
 - » **Unused Blood Handling:** Return unused blood to the blood bank within 30 minutes.
 - » **Avoid Warming:** Prevent adverse reactions by avoiding the warming of blood.

2. FRESH FROZEN PLASMA (FFP)

- **Volume:** 200 – 250 mL per unit.
- **Content:** Contains clotting factors, albumin, immunoglobulins, and other plasma proteins.
- **Storage:** Must be stored at -18°C or lower
- **Shelf life:** For up to 12 months
- **Indication:**
 - » Used to treat coagulation factor deficiencies, liver disease, DIC, massive transfusions, and other conditions requiring replacement of multiple coagulation factors.
 - » Administered for warfarin overdose.
 - » Used to replenish coagulation factors during massive transfusions.
 - » Employed in cases of Disseminated Intravascular Coagulation (DIC).
 - » Utilized in the treatment of Thrombotic Thrombocytopenic Purpura (TTP).
 - » Applied in snakebite cases for correction of INR.
- **Special instruction:**
 - » **Dosage:** 15 mL/kg x body weight
 - » **ABO Compatibility:** Consider checking required.
 - » **Cross-matching:** Not needed; complete transfusion within 30 mins.
 - » **Thawing (warming a frozen substance):** Between 30°C to 37°C.
 - » **Storage:** Thawed plasma at 2°C – 6°C.
 - » **Effect:** One unit increases Hb by about 1.0 g/dL.
 - » **Complications:** Hemochromatosis with chronic transfusions.
 - » **Warning:** Use within 6 hours of thawing; never refreeze.



3. PLATELETS CONCENTRATES

- **Volume:**
 - » Platelet concentrate: 50 – 70 mL per units.
 - » Platelet pheresis concentrate: 150 – 300 mL per units.
- **Unit issue**
 - » Platelet concentrate: range from 4 to 6 random donor units.
 - » Platelet pheresis concentrate: single pack contains one therapeutic unit.
- **Storage:** Stored at room temperature (20°C – 24°C) with continuous agitation to prevent clotting, usually on an agitator for up to 5 days
- **Shelf life:** 5 days from the date of collections.
- **Indication:**
 - » Thrombocytopenia to prevent spontaneous bleeding.
 - » Coagulopathy, or platelet dysfunction (Platelet function defects)
 - » Massive blood loss
- **Contraindication:**
 - » Hypersensitivity to platelet products.
 - » Active bleeding from Disseminated intravascular coagulation (DIC).
 - » Idiopathic thrombocytopenic purpura (ITP).
 - » Thrombotic thrombocytopenic purpura (TTP).
 - » Thrombocytopenia is associated with septicemia.
 - » Hypervolemia or fluid overload.
- **Special instruction:**
 - » **Dosage: Platelet concentrate:** One unit of platelet concentrate per 10 kg body weight, typical 4 – 6 single donor units for a therapeutic dose in adults weighing 60-70 kg. **Platelet pheresis concentrate:** One unit of platelet pheresis concentrate (mega unit = 1 adult dose)
 - » **Compatibility:** Preferably ABO matched; Cross-matching not required.
 - » **Administration:** Begin transfusion promptly; Complete within 30 minutes.
 - » Do not refrigerate, platelets products as this reduces platelet functions.
 - » **Effect:** per unit increases platelet count by approx. 20-40/nL.

4. CRYOPRECIPITATE

- **Content:** High level of clotting factors (fibrinogen, factor VIII, XIII), vWF, and Fibronectin
- **Indications:** similar to FFP; used to treat bleeding disorders or conditions associated with low levels of fibrinogen, such as hypofibrinogenemia, dysfibrinogenemia, or fibrinogen deficiency, preferable if large transfusion volumes are undesirable or during surgical procedures where fibrinogen replacement is necessary.

5. CLOTTING FACTORS

- **Content:** specific clotting factors that have been pooled from multiple donors. They include factor such as prothrombin complex concentrate, factor VIII, factor IX, and factor XIII.
- **Indications:** specific clotting factors, such as hemophilia-A (factor VIII deficiency) and hemophilia-B (factor IX deficiency), life-threatening bleeds or during surgery to prevent excessive bleeding and warfarin overdose.

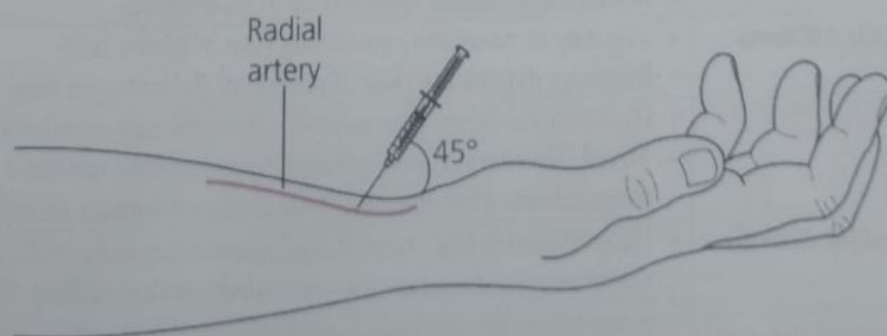
6. ANTITHROMBIN-III (AT-III)

- **Contents:** Antithrombin-III (AT-III) is a plasma protein that inhibits coagulation process, which is synthesized in the liver → inhibition of thrombin, Xa, IXa, Xa.
- **Effect:** increases the effects of heparin
- **Indication:**
 - Used to treat or prevent blood clots in patients with congenital or acquired antithrombin deficiency (E.g. hereditary AT-III deficiency to prevent thrombosis prophylaxis with heparin)
 - Used in Thromboembolism and disseminated intravascular coagulation (DIC) if indicated.

ARTERIAL BLOOD GAS (ABG) SAMPLING

- ☞ Introducing yourself to the patient and confirming their name and age for identification.
- ☞ Provide a clear explanation of the procedure and obtain informed consent from the patient.
- ☞ **Gather the Equipment:** Gather all necessary equipment required for the procedure.

» A pair of non-sterile gloves	» Needles or syringe (heparinized).
» An alcohol wipe and cotton wool	» ABG collection kit or green top vacutainer tube
» Tourniquet	» An adhesive plaster or clear dressing.
- ☞ **Hand Hygiene:** Thoroughly wash and dry your hands to maintain a sterile environment.
- ☞ **Gloves application:** Put on sterile gloves to prevent contamination during the procedure.
- ☞ **Patient Positioning:** Position the patient comfortably, typically in a supine or semi-Fowler's position. Ensure the patient's arm is extended and supported at heart level to facilitate blood flow.
- ☞ **Site Preparation:** Identify the puncture site, usually the radial artery at the wrist, by palpating for the pulse. An alternative site is the femoral artery. Assess collateral circulation by performing Allen's test (see below Box). Clean the skin using alcohol wipes using circular motion and allow it to dry.
- ☞ **ABGs Procedure:**
 1. Perform hand hygiene and put on sterile gloves to prevent contamination during the procedure.
 2. Clean the skin using alcohol wipes using circular motion and allow it to dry.
 3. Palpate the artery with the index and middle finger to locate the pulse. Hold the syringe at a 45-degree angle, bevel up, immediately next to the tip of the index finger, and insert the needle smoothly and swiftly into the artery at the puncture site along the line of the pulse. Once the artery is punctured, gently pull back on the plunger to aspirate an adequate blood sample into the syringe.
 4. Fill the syringe with the required amount of arterial blood, typically 1-2 mL, depending on the test requirements. Avoid excessive agitation of the sample to prevent hemolysis.
 5. Release the tourniquet to restore normal blood flow, withdraw the needle and apply pressure to the puncture site at least 5 minutes or until bleeding stops, while ensuring the patient's comfort.
 6. Label the heparinized syringe or green top vacutainer bottle with patient identification information, date, age and time of collection. Fill in the blood request form (at least: patient's name, date of birth, and hospital number; date of blood collection; tests required e.g. ABGs).
 7. Transport the arterial blood sample promptly to the laboratory for analysis. Maintain sample integrity by using ice water or ice cubes for cooling during transportation. Ensure proper handling and storage throughout the process.
 8. Assess the puncture site for signs of bleeding or hematoma formation.
- ☞ Ensure the patient's comfort throughout the procedure. Monitor the patient for signs of distress or discomfort during the procedure. Provide reassurance and support as needed.
- ☞ **Gratitude:** Thank the patient for their cooperation.
- ☞ **Documentation:** Document the details of the procedure including the site, amount of blood collected, and any complications encountered, in the patient's medical record.
- ☞ **Waste Disposal:** Dispose of all used materials appropriately to maintain cleanliness and safety.



Angle of insertion of needle for arterial blood gas sampling

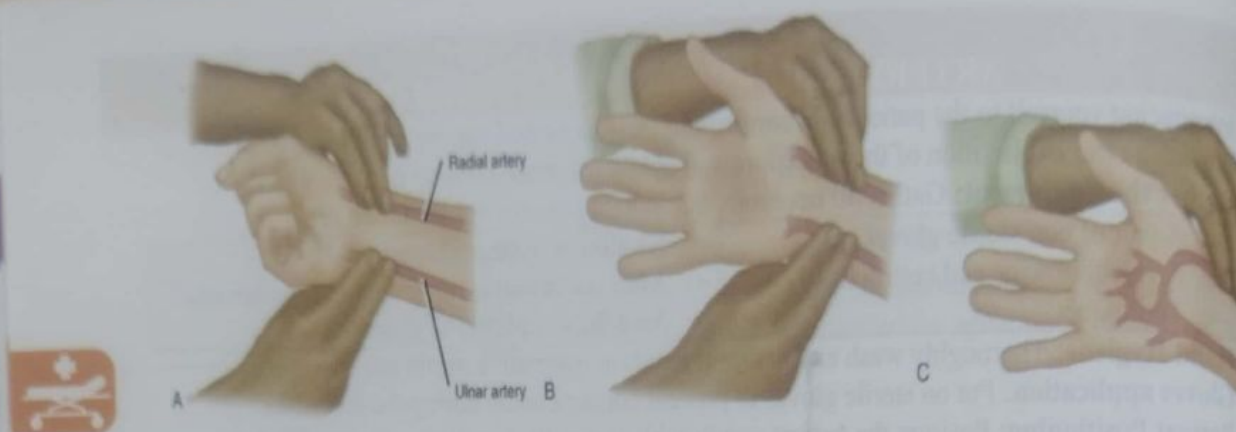


FIGURE: MODIFIED ALLEN TEST

- A. The hand is clenched into a tight fist, and pressure is applied to the radial and ulnar arteries.
 B. The hand is opened (but not fully extended); the palm and fingers are blanched.
 C. Removal of pressure on the ulnar artery should result in flushing of the entire hand (within 5 to 10 seconds) indicative of adequate collateral circulation or a normal modified Allen test.

ARTERIAL BLOOD GAS (ABG) INTERPRETATION

Normal values for arterial blood gas (ABG) components at sea level are

Hypoxemia	⚡ ↓	Partial pressure of oxygen (PaO ₂): 75 – 100 mmHg	↑ ⚡	O ₂ toxic
ACID	⚡ ↓	pH (potential of hydrogen): 7.35–7.45	↑ ⚡	BASE
BASE	⚡ ↓	PaCO ₂ (Partial Pressure of Carbon Dioxide): 35 – 45 mmHg	↑ ⚡	ACID
ACID	⚡ ↓	HCO ₃ ⁻ (Bicarbonate): 22 – 28 mEq/L	↑ ⚡	BASE

DISORDER	pH	HCO ₃	PCO ₂
METABOLIC ACIDOSIS	DECREASE	DECREASE	DECREASE
METABOLIC ALKALOSIS	INCREASE	INCREASE	DECREASE
RESPIRATORY ACIDOSIS	DECREASE	INCREASE	INCREASE
RESPIRATORY ALKALOSIS	INCREASE	DECREASE	DECREASE

COMMON CAUSES OF ACID BASE DISORDERS

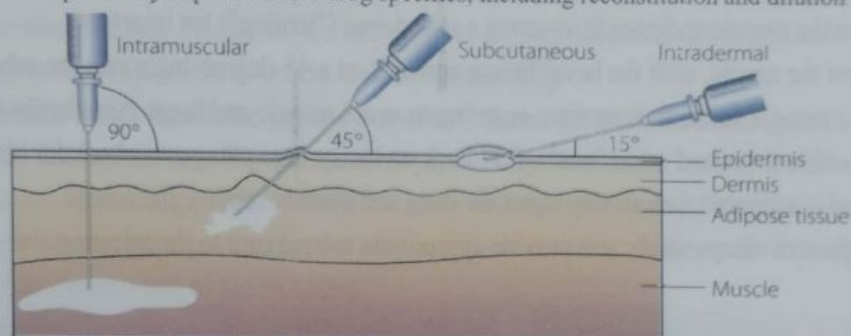
1. Metabolic Acidosis	» Diabetic ketoacidosis (DKA), Salicylate poisoning » Lactic acidosis (e.g., sepsis, shock, tissue hypoxia) » Renal failure (accumulation of metabolic acids) » Diarrhea or intestinal fistulas (loss of bicarbonate)
2. Metabolic Alkalosis	» Vomiting or nasogastric suctioning (loss of gastric acid) » Excessive diuretic use (loss of potassium and hydrogen ions) » Hyperaldosteronism, Excessive use of bicarbonate-containing antacids » Mixed Disorders: Combination of respiratory and metabolic abnormalities, often seen in critical illness or complex clinical conditions
3. Respiratory Acidosis	» Hypoventilation (e.g., respiratory depression, opioid overdose, neuromuscular diseases). Airway obstruction (e.g., asthma, COPD exacerbation, foreign body aspiration)
4. Respiratory Alkalosis	» Hyperventilation (e.g., anxiety, pain, fever, sepsis, hypoxemia) » Mechanical ventilation with high respiratory rates

INJECTION METHOD (INTRAMUSCULAR, SUBCUTANEOUS & INTRADERMAL)

PREPARATION

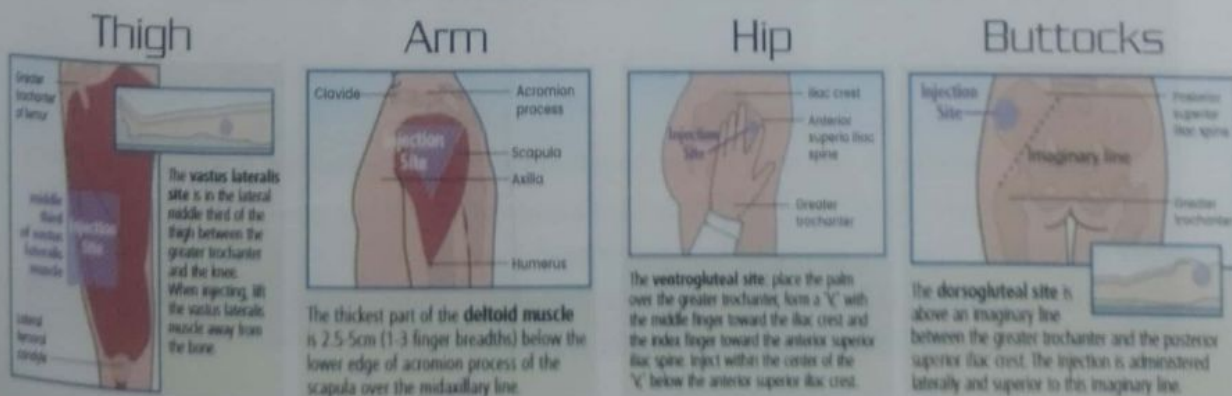
- ☞ Introducing yourself to the patient and confirming their name and age for identification.
- ☞ Provide a clear explanation of the procedure and obtain informed consent from the patient.
- ☞ **Gather the Equipment:** Gather all necessary equipment required for the procedure.

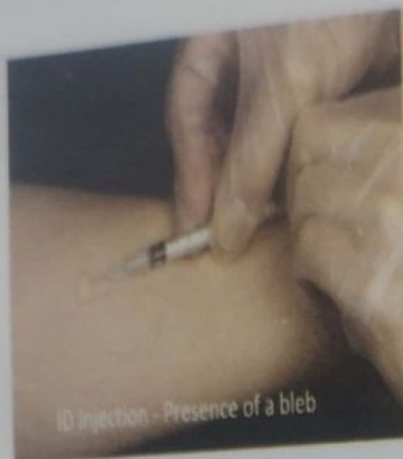
» A pair of non-sterile gloves	» Needles or Syringe (Heparinized).
» An alcohol wipe and cotton wool	» Medication vial or ampoule
» Tourniquet	» An adhesive plaster or clear dressing.
- ☞ Ask the patient about any allergies and reactions they may have experienced and inquire about the nature of their reactions if they occur.
- ☞ Check the prescription chart for patient details, drug name, dose, diluent (if needed), route of administration, date, and time of administration, and verify any drug allergies or anticoagulant therapy. Double-check the drug name, dose, and expiry date on the vial.
- ☞ Consult the local pharmacy department for drug specifics, including reconstitution and dilution requirements.



INTRAMUSCULAR (IM) INJECTION METHOD

1. Perform hand hygiene and put on sterile gloves to prevent contamination during the procedure.
2. Clean the skin using alcohol wipes or chlorhexidine sponges and allow it to dry.
3. **Location:** Locate an appropriate muscle for injection, such as the deltoid, vastus lateralis, or dorsogluteal. In older children and adults, the deltoid muscle, specifically the densest portion above the armpit and below the acromion, is preferred for IM injections. Avoid the gluteal muscle due to needle reach limitations and the risk of sciatic nerve damage. For infants and toddlers, the vastus lateralis muscle in the anterolateral aspect of the thigh is the recommended IM injection site.
4. With your free hand, slightly stretch the skin at the site of injection.
5. Insert the needle at a 90-degree angle into the muscle. Pull back on the syringe plunger to check for blood return, if no bleed is aspirated then slowly inject the drug and quickly remove the needle.
6. Dispose of sharps safely and provide appropriate wound care to the injection site.

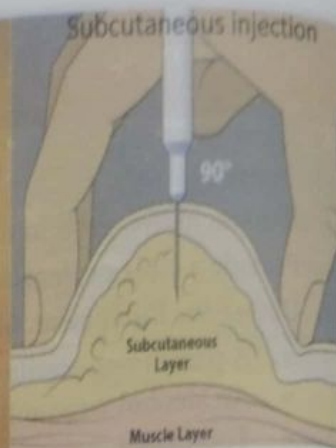




ID Injection - Presence of a bleb



Draw circle around injection site



Subcutaneous injection

Subcutaneous Layer

Muscle Layer

SUBCUTANEOUS (SC) INJECTION METHOD

1. Perform hand hygiene and put on sterile gloves to prevent contamination during the procedure.
2. Clean the skin using alcohol wipes or chlorhexidine sponges and allow it to dry.
3. Gently pinch the skin at the chosen site between the thumb and forefinger to lift the adipose tissue from the muscle underneath, creating a raised area ("tenting") for injection.
4. Insert the needle, with the bevel facing upwards, at a 45-degree angle into the subcutaneous tissue (SC) using a quick, firm motion, ensuring to avoid muscle and bone. Aim for the tip of the needle to be within the raised area ("tent"). Pull back on the syringe plunger to check for blood return, if no bleed is aspirated then slowly inject the drug and quickly remove the needle.
5. Dispose of sharps safely and provide appropriate wound care to the injection site.

INTRADERMAL (ID) INJECTION METHOD

1. Perform hand hygiene and put on sterile gloves to prevent contamination during the procedure.
2. Clean the skin using alcohol wipes or chlorhexidine sponges and allow it to dry.
3. Insert the needle almost parallel to the skin at a shallow angle (5 to 15 degrees), ensuring the bevel is facing upwards. Stretch the skin taut between thumb and forefinger, making the needle visible beneath the surface of the epidermis. Slowly inject a small amount of medication (typically 0.1 to 0.2 mL) into the dermal layer, forming a small wheal or bleb.
4. Verify the formation of a visible (and sometimes uncomfortable) bleb; if not, withdraw the needle immediately and retry, as it may have been inserted too deeply then slowly inject the drug and quickly remove the needle.
5. Do not massage or rub the injection site. Monitor for any localized reactions or signs of infection.
6. Dispose of sharps safely and provide appropriate wound care to the injection site.

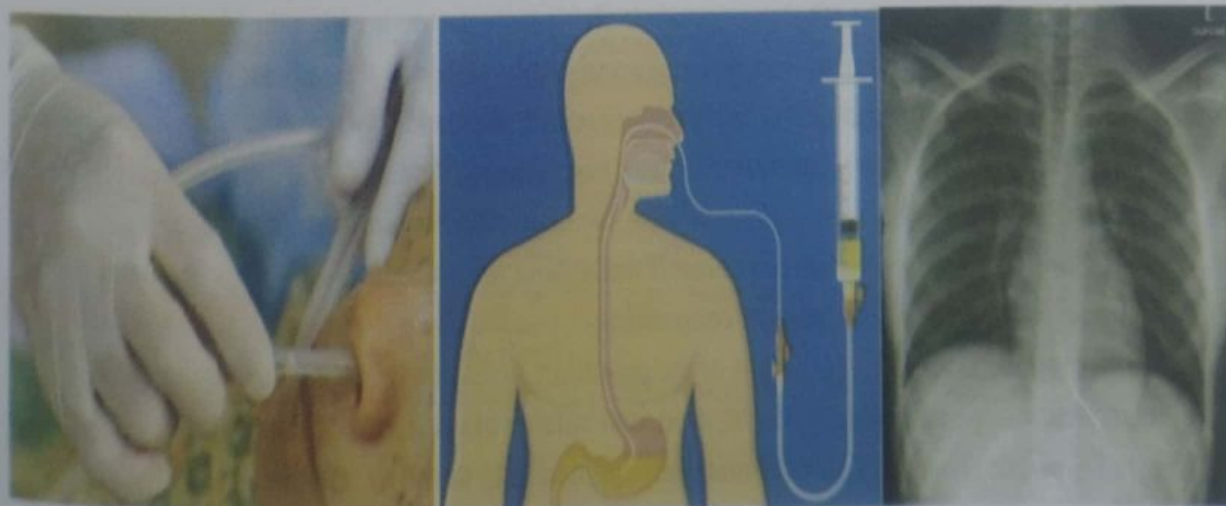
PATIENT CARE & CONCERN

- ☞ **Patient's comfort & concerns:** Ensure the patient's comfort throughout the procedure. Ask if they have any questions or concerns. Provide reassurance and support as needed.
- ☞ **Gratitude:** Thank the patient for their cooperation.
- ☞ **Documentation:** Document the details of the procedure including record the date, time, drug, dose, and injection site of the injection and sign the prescription chart.

NASOGASTRIC (NG) TUBE INTUBATION

- ☞ Introducing yourself to the patient and confirming their name and age for identification.
- ☞ Provide a clear explanation of the procedure and obtain informed consent from the patient.
- ☞ **Gather the Equipment:** Gather all necessary equipment required for the procedure.

» A pair of non-sterile gloves	» Stethoscope (for confirming tube placement)
» Appropriate size nasogastric (NG) tube	» pH strips or litmus paper (if necessary)
» Lubricant (water-soluble gel or liquid)	» Water or saline solution (for swallowing test)
» Lignocaine gel (for local anesthesia)	» Straw (for swallowing test)
» Syringe and spigot or catheter bag	» An adhesive plaster or clear dressing.
- ☞ **Hand Hygiene:** Thoroughly wash and dry your hands to maintain a sterile environment.
- ☞ **Gloves application:** Put on sterile gloves to prevent contamination during the procedure.
- ☞ **Positioning:** Place patient in a semi-upright position (45-60 degrees) to ease insertion and reduce the risk of aspiration. Additionally, examine both nostrils for optimal tube placement.
- ☞ **Preparation of Tube:** Measure the length of NG tube to be inserted by placing the tip of the tube at the nostril and extending the tube behind the ear and then to two fingerbreadths above the umbilicus. Lubricate the distal end (tip) of the NG tube with Xylocaine jelly.
- ☞ **Insertion methods:** Instill lignocaine gel into one nostril. Insert the lubricated tube into the nostril and slide it along the floor of the nose into the nasopharynx aiming towards the back of the throat. Gradually advance, instructing patient to swallow water with each movement. Stop if resistance is felt. If patient coughs or gags, gently withdraw the tube and allow recovery. Secure tube with adhesive tape. Attach a spigot or catheter bag to the NG tube.
- ☞ **Confirmation:** Confirm correct placement by checking pH, aspirating gastric contents, or performing X-ray. Ensure the tube's tip is in the stomach by injecting 20 ml of air and listening over the epigastrium with a stethoscope.
- ☞ **Patient's comfort & concerns:** Ensure the patient's comfort throughout the procedure. Ask if they have any questions or concerns. Provide reassurance and support as needed.
- ☞ **Gratitude:** Thank the patient for their cooperation.
- ☞ **Documentation:** Document the details of the procedure including record the date, time and confirming that the NG tube has been successfully placed.
- ☞ **Waste Disposal:** Dispose of all used materials appropriately to maintain cleanliness and safety.



URINARY CATHETERIZATION

- ☞ Introducing yourself to the patient and confirming their name and age for identification.
- ☞ Provide a clear explanation of the procedure and obtain informed consent from the patient.
- ☞ **Gather the Equipment:** Gather all necessary equipment required for the procedure.

» A pair of non-sterile gloves	» Syringe and catheter bag or urine bag.
» Appropriate size Foley catheter	» A 10 ml syringe containing sterile water (never use normal saline for inflation)
» Lubricant (water-soluble gel or liquid)	» An adhesive plaster or clear dressing.
» Lignocaine gel (for local anesthesia)	

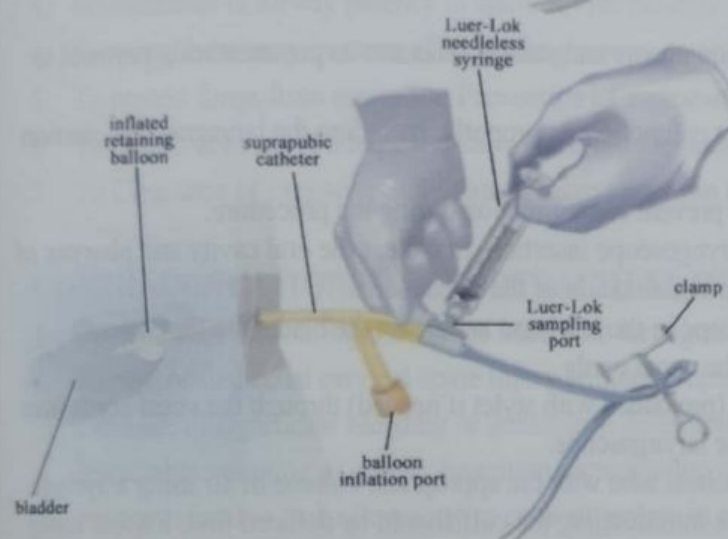
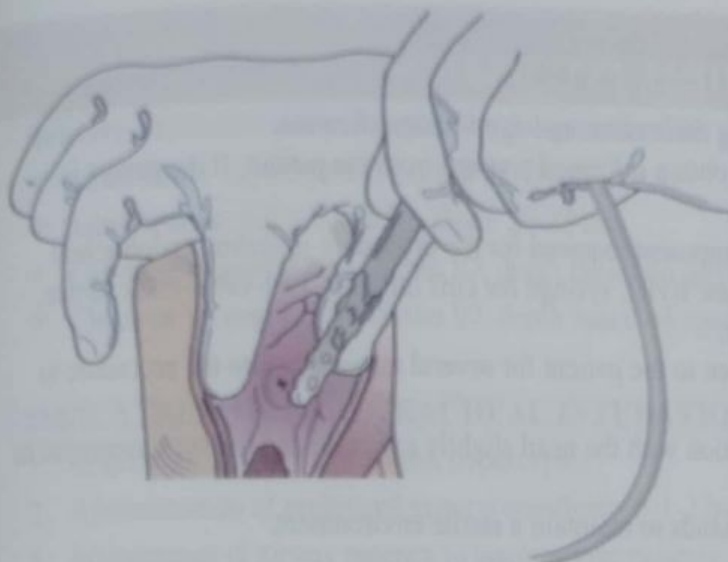
- ☞ **Hand Hygiene:** Thoroughly wash and dry your hands to maintain a sterile environment.
- ☞ **Gloves application:** Put on sterile gloves to prevent contamination during the procedure.
- ☞ **Positioning:** Position the patient supine, lying on their back with legs spread apart.
- ☞ **Inflation:** Draw up 10 ml sterile water for inflation. Avoid saline solution. Inflating a urinary catheter balloon with saline solution can lead to tissue irritation and catheter malfunction.
- ☞ **Lubrication:** Draw up 3 – 5 mL of lignocaine gel in syringe. Inform the patient of a 5-minute waiting period for the lignocaine to take effect.
- ☞ **Genital Cleaning:** Clean the genital area with saline-soaked swabs.
- ☞ **Insertion method:**

1. **In Men:** Warn the patient you are about to insert the catheter. Hold the penis vertically using a piece of sterile gauze. Instill 3-5 mL of lignocaine gel into the urethra for lubrication. Insert the lubricated catheter into the urethral opening. Advance the catheter until it is fully inserted into the penis. As you enter the bladder, urine should begin to drain from the catheter. Once the catheter is fully inserted, inflate the catheter balloon with the 10ml syringe of sterile water to secure it within the bladder. Once the balloon is fully inflated, remove the syringe and gently withdraw the catheter until resistance is noted, confirming the catheter is held securely within the bladder.
2. **In Women:** Warn the patient you are about to insert the catheter. Separate the labia minora. Instill 3-5 mL of lignocaine gel into the urethra for lubrication. Insert the lubricated catheter into the urethral opening. Advance the catheter until it is fully inserted into the urethra. As you enter the bladder, urine should begin to drain from the catheter. Once the catheter is fully inserted, inflate the catheter balloon with the 10ml syringe of sterile water to secure it within the bladder. Once the balloon is fully inflated, remove the syringe and gently withdraw the catheter until resistance is noted, confirming the catheter is held securely within the bladder.

- ☞ **Attaching the catheter bag:** Attach the catheter bag tubing to the end of the catheter securely. Position the catheter bag below the level of the patient to facilitate effective drainage of urine.
- ☞ **Patient Comfort:** Ensure the patient's comfort throughout the procedure.
- ☞ **Gratitude:** Thank the patient for their cooperation.

Documentation: Document the details of the procedure including recording the date and time of catheterisation, type and size of catheter used, and volume of urine in the catheter bag.

- ☞ **Waste Disposal:** Dispose of all used materials appropriately to maintain cleanliness and safety.



INDICATIONS

1. Hygienic care of bedridden patients
2. Acute urinary retention
3. Perioperative management
4. Accurate measurement of urine output in critically ill patients
5. Monitoring urine output in patients with kidney dysfunction or fluid balance issues
6. Chronic urinary obstruction or bladder outlet obstruction
7. Collection of a specimen of uncontaminated urine.
8. Irrigation of the bladder.
9. Imaging of the urinary tract.

CONTRAINDICATIONS

1. Pelvic trauma: urethral trauma or injury, such as recent urethral surgery or suspected urethral rupture.
2. Suspected or confirmed urethral obstruction, such as urethral strictures or blood clots.
3. Active urinary tract infection (UTI) or epididymitis, as catheterization may exacerbate the infection or spread bacteria into the bladder or bloodstream.
4. Recent instrumentation or manipulation of the lower urinary tract
5. Previous failure to catheterize.
6. Severe phimosis.

COMPLICATIONS

1. Paraphimosis (from failure to reposition the foreskin).
2. Urethral trauma or urethral perforation and creation of false passages.
3. Bleeding.
4. Infection.
5. Urinary retention.
6. Urethral strictures.

ENDOTRACHEAL INTUBATION

- ☞ Introducing yourself to the patient and confirming their name and age for identification.
- ☞ Provide a clear explanation of the procedure and obtain informed consent from the patient. If the patient is unconscious, obtain consent from the next of kin.
- ☞ **Gather the Equipment:** Gather all necessary equipment required for the procedure including endotracheal tubes of appropriate size, laryngoscope with blades, stylet, syringe for cuff inflation, bag-valve-mask device, suction catheter, and adhesive tape or tube holder.
- ☞ **Preoxygenation:** Administer supplemental oxygen to the patient for several minutes before the procedure to increase oxygen reserves in the lungs.
- ☞ **Positioning:** Position the patient in a supine position with the head slightly extended and the neck supported to align the airway and facilitate visualization.
- ☞ **Hand Hygiene:** Thoroughly wash and dry your hands to maintain a sterile environment.
- ☞ **PROCEDURE**
 1. **Induction of Anesthesia:** Administer induction agents and muscle relaxants as per anesthesia protocol to induce unconsciousness and muscle relaxation.
 2. **Equipment Check:** Ensure that all equipment is functioning properly, including the laryngoscope, suction device, and bag-valve-mask device.
 3. **Gloves applications:** Put on sterile gloves to prevent contamination during the procedure.
 4. **Clearing the Airway by Suction:** Prior to laryngoscope insertion, first clear the oral cavity and pharynx of secretions using a suction catheter to optimize visualization of the vocal cords.
 5. **Laryngoscope Insertion:** Hold the laryngoscope in the left hand and insert the blade into the patient's mouth, gently lifting the tongue to visualize the vocal cords.
 6. **Tube Insertion:** Insert the endotracheal tube (preloaded with stylet if needed) through the vocal cords into the trachea under direct visualization using the laryngoscope.
 7. **Cuff Inflation:** Inflate the cuff of the endotracheal tube with the appropriate volume of air using a syringe to create a seal within the trachea. **N.B.** Before introduction, the cuff should be deflated first. Rubber tubes are used for shorter durations, up to 24 hours, due to their potential for irritation. Portex tubes, made of polyethylene, cause less irritation, and can remain in place for up to 7 days.
 8. **Confirmation:** Confirm proper tube placement by observing chest rise and auscultating bilateral breath sounds. Use capnography to verify CO₂ detection in exhaled breath.
Confirmation of correct endotracheal tube placement: 1. Visual confirmation during intubation. 2. Bilateral chest rise observed. 3. Bilateral equal breath sounds auscultated. 4. Absence of breath sounds in the epigastrium. 5. Normal capnography waveform (square wave). 6. Prompt inflation of deflated esophageal detector device bulb. 7. Chest X-ray to verify tube placement, if available.
 9. **Securing the Tube:** Secure the endotracheal tube (ETT) in place with adhesive tape or a tube holder to prevent accidental dislodgment.
 10. **Oxygenation and Ventilation:** Begin mechanical ventilation using the bag-valve-mask device connected to the endotracheal tube to ensure adequate oxygenation and ventilation.
 11. **Monitoring:** Continuously monitor vital signs, oxygen saturation, end-tidal CO₂, and cardiac rhythm to assess the patient's condition and response to intubation.
 12. **Position Confirmation:** Reconfirm endotracheal tube placement periodically during transport and upon arrival at the destination, such as the intensive care unit or operating room.
 13. **Post-Intubation Care:** Provide ongoing airway management and support as needed, including suctioning of secretions, cuff pressure monitoring, and periodic repositioning of the patient.
 14. **Handoff:** Provide a thorough handoff report to the receiving healthcare team, including details of the intubation procedure and the patient's status.
- ☞ **Patient Comfort:** Ensure the patient's comfort throughout the procedure.
- ☞ **Monitoring:** Ensure the patient's comfort throughout the procedure. Monitor the patient for signs of distress or discomfort during the procedure. Provide reassurance and support as needed.
- ☞ **Gratitude:** Thank the patient for their cooperation.
- ☞ **Documentation:** Document the details of the procedure including the amount, color, and consistency of the aspirated fluid for accurate record-keeping and analysis purposes.
- ☞ **Waste Disposal:** Dispose of all used materials appropriately to maintain cleanliness and safety.

ENDOTRACHEAL TUBE SIZES

Endotracheal tubes (ETT) are available in different sizes. Their size is indicated as the internal diameter in mm. However, the correct size will depend on the growth of the child.

- **Adult male:** 7.0-8.5 mm ID, depth 21-24 cm
- **Adult female:** 6.0-8.0 mm ID, depth 20-23 cm
- **Children >6 years:** 6.0-7.5 mm ID, depth based on age/height.
- **Children <6 years:** 3.0-5.5 mm ID, depth based on age/weight.

INDICATIONS OF ENDOTRACHEAL INTUBATION

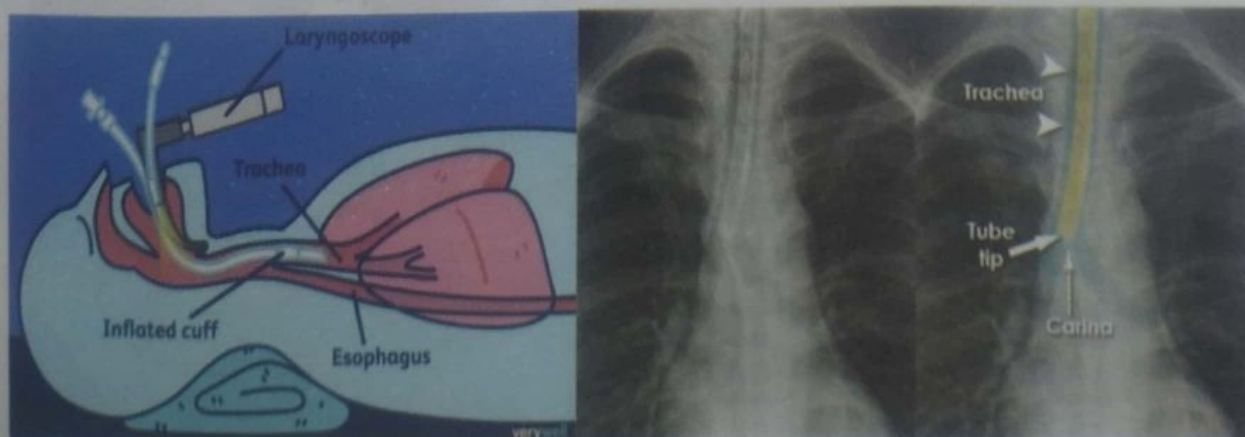
1. Respiratory failure (hypoxemic, hypercapnic)
2. Administration of prolonged general anesthesia (>1-2 hours)
3. Maintenance of airway patency in unconscious patients
4. Securing the airway in cases of impending airway compromise (e.g., trauma, head trauma, angioedema)
5. To protect lungs from aspiration/Prevention of aspiration of regurgitated gastric contents
6. To ensure delivery of adequate tidal volumes to the lungs.
7. To Clearance of excessive and retained secretions from the lungs.

CONTRAINDICATIONS OF ENDOTRACHEAL INTUBATION

1. Severe facial trauma, Injuries to the neck with laryngeal rupture, large tumours of the upper airway.
2. Known or suspected cervical spine injury without proper stabilization
3. Presence of significant bleeding or anatomical distortion hindering visualization of the airway structures
4. Intractable vomiting or gastric distention increases the risk of aspiration during intubation.
5. Patient refusal or lack of capacity to consent, unless in a life-threatening situation with no alternative means of airway management

COMPLICATIONS OF ENDOTRACHEAL INTUBATION

- **Immediate complications**
 - **Airway trauma:** trauma to teeth, lips, tongue, pharynx, or larynx
 - Haemodynamic changes-tachycardia (Arrhythmias), hypertension, myocardial ischaemia, hypoxemia
 - Misplaced tube-accidental extubation, oesophageal intubation, aspiration, Laryngeal edema
- **Delayed complications:**
 - Laryngeal granuloma, laryngeal stenosis, or subglottic stenosis
 - Ventilator-associated pneumonia, Tracheal stenosis, Vocal cord dysfunction
 - Barotrauma, Mucosal ulceration, and Tube-related issues



STERILE SUCTIONING PROCEDURE

- ☞ Introducing yourself to the patient and confirming their name and age for identification.
- ☞ Provide a clear explanation of the procedure and obtain informed consent from the patient.
- ☞ **Gather the Equipment:** Gather all necessary equipment required for the procedure.

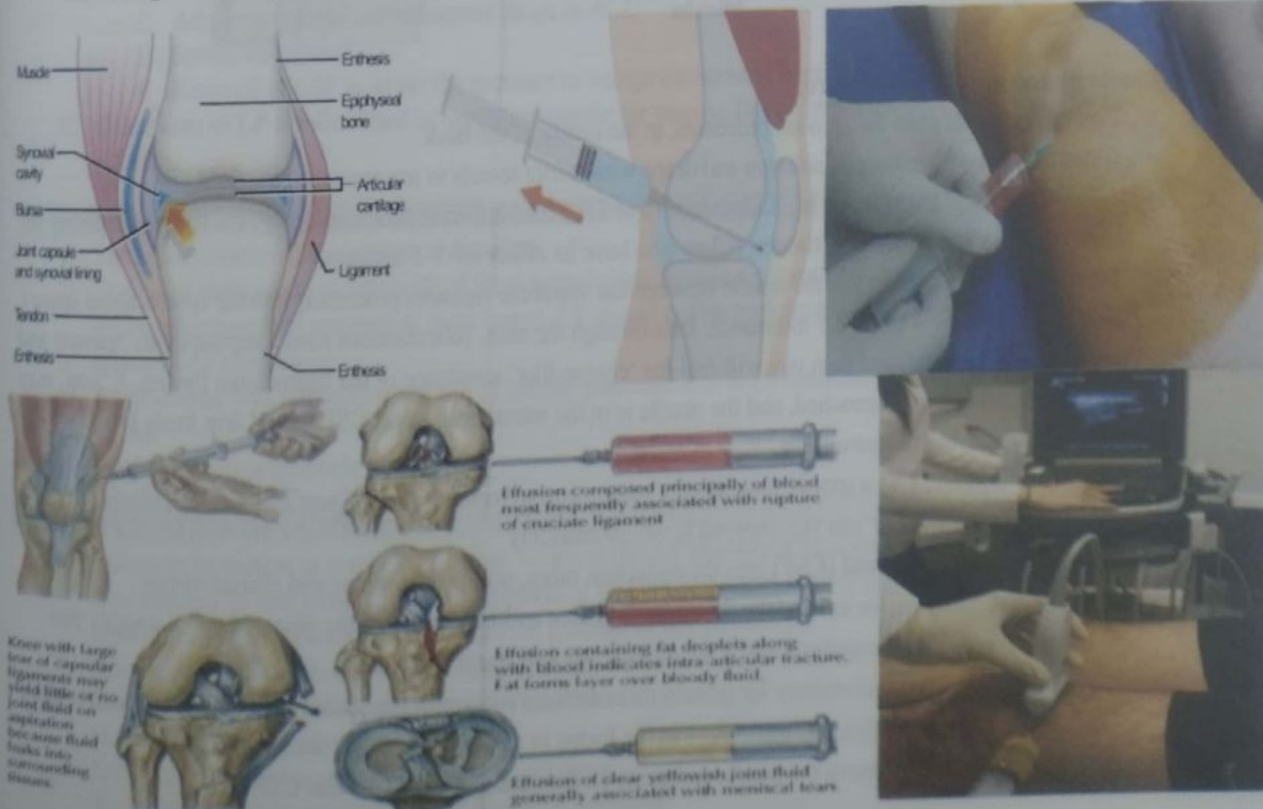
» Suction apparatus.	» Waste disposal container.
» Sterile suction catheter	» Suction control device.
» Sterile saline solution	» Lubricant (if needed)
» Sterile gloves	» Additional catheters (if necessary)
» Towels or disposable under pads.	» Basin for sterile saline
» Personal protective equipment (PPE)	» Additional assistance or aid required

- ☞ **Hand Hygiene:** Thoroughly wash and dry your hands to maintain a sterile environment.
- ☞ **Gloves application:** Put on sterile gloves to prevent contamination during the procedure.
- ☞ **Procedure:**
 1. **Suction Apparatus Assembly:** Ensure the suction apparatus is properly assembled and functional. Attach a clean suction catheter of appropriate size to the suction tubing.
 2. **Patient Positioning:** Position the patient comfortably with their head tilted slightly backward for easy access to the oral cavity.
 3. **Catheter Insertion:** Gently insert the suction catheter into the mouth, avoiding contact with the back of the throat to prevent triggering the gag reflex.
 4. **Suction Technique:** Apply intermittent suction by depressing the suction control button or valve while slowly withdrawing the catheter. Rotate the catheter slightly during withdrawal to thoroughly suction secretions from all areas of the oral cavity.
 5. **Catheter Maintenance:** Rinse the suction catheter with sterile saline solution between each suction pass to maintain cleanliness and prevent cross-contamination. Repeat suctioning as necessary until the oral cavity is clear of secretions.
- ☞ **Patient Comfort & Monitoring:** Ensure the patient's comfort throughout the procedure. Monitor the patient for signs of distress or discomfort during suctioning. Provide reassurance and support as needed.
- ☞ **Gratitude:** Thank the patient for their cooperation.
- ☞ **Documentation:** Document the details of the procedure including the amount, color, and consistency of the aspirated fluid for accurate record-keeping and analysis purposes.
- ☞ **Waste Disposal:** Dispose of all used materials appropriately to maintain cleanliness and safety.



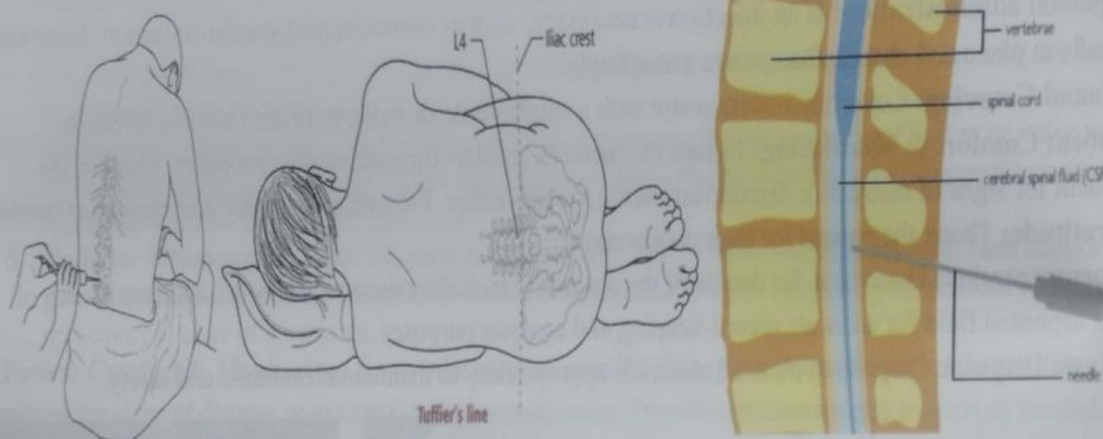
KNEE ARTHROCENTESIS (KNEE JOINT ASPIRATION)

- ☞ Introducing yourself to the patient and confirming their name and age for identification.
- ☞ Provide a clear explanation of the procedure and obtain informed consent from the patient.
- ☞ Position the patient comfortably on a bed with proper support for the targeted joint, such as the knee.
- ☞ **Equipment collection:** Gather all necessary equipment required for the procedure.
- ☞ **Hand Hygiene:** Thoroughly wash and dry your hands to maintain a sterile environment.
- ☞ **Gloves application:** Put on sterile gloves to prevent contamination during the procedure.
- ☞ **Marking and Cleaning:** For knee aspiration, utilize a lateral approach. Mark a line on the lateral edge of the patella between the upper and middle thirds, aiming 1-2 cm below this point for needle insertion. Clean the marked area with chlorhexidine solution, starting from the center and moving outward. Allow it to dry.
- ☞ **Skin preparation:** Apply refrigerant alcohol spray to the marked needle insertion point to numb the area, minimizing discomfort during the procedure.
- ☞ **Needle insertion:** Use a green needle and insert it at a 90° angle to the skin, aiming between the patella and femoral condyle. Gradually insert the needle while aspirating until joint fluid is successfully obtained.
- ☞ **Fluid collection:** Collect the necessary amount of fluid for analysis or symptomatic relief, ensuring thorough extraction until dryness is achieved if needed.
- ☞ **Optional administration:** If an injection is necessary, such as corticosteroid steroids injection, leave the needle in place and change the syringe accordingly.
- ☞ **Wound Covering:** Cover the insertion site with a small sterile dressing to protect against infection.
- ☞ **Patient Comfort & Monitoring:** Ensure the patient's comfort throughout the procedure. Monitor the patient for signs of distress or discomfort during the procedure. Provide reassurance and support as needed.
- ☞ **Gratitude:** Thank the patient for their cooperation.
- ☞ **Documentation:** Document the details of the procedure including the amount, color, and consistency of the aspirated fluid for accurate record-keeping and analysis purposes.
- ☞ **Waste Disposal:** Dispose of all used materials appropriately to maintain cleanliness and safety.



LUMBER PUNCTURE (SPINAL TAP)

- ☞ Introducing yourself to the patient and confirming their name and age for identification.
 - ☞ Provide a clear explanation of the procedure and obtain informed consent from the patient.
 - ☞ **Gather the Equipment:** Gather all necessary equipment required for the procedure.
 - ☞ **Hand Hygiene:** Thoroughly wash and dry your hands to maintain a sterile environment.
 - ☞ **Gloves application:** Put on sterile gloves to prevent contamination during the procedure.
 - ☞ **Location & Positioning:** Choose between the lateral decubitus position or the sitting position.
1. **First choice – Lateral Decubitus Position:** Initial choice, safer, and enables CSF pressure measurement. Instruct patients to assume the knee-chest position by lying on their left side with knees pulled up to their chest and chin tucked. This position helps to open the spaces between the vertebrae, making it easier to access the lumbar area, facilitating needle insertion and promoting relaxation.
 2. **Second choice – Sitting Position:** This position carries a greater risk of herniation and does not allow for CSF pressure measurement; it can be considered in specific circumstances. Instruct the patient to sit upright and lean forward over a bedside table. This position allows access to the lumbar area and may be preferable for patients with respiratory issues or when immediate CSF drainage is necessary.
 3. **Location:** Usually between the L3/L4 or L4/L5 vertebrae. Locate Tuffier's line, an imaginary line between the iliac crests, which corresponds to approximately L4.

☞ **Lumbar puncture (LP) procedure:**

- » Feel the space between the spinous processes, in the centre of the back.
- » Clean the area with antiseptic solution and drape with sterile towels to maintain a sterile field.
- » **Administer local anesthesia:** Inj. Lidocaine 2% at 5–10 mL, infiltrate subcutaneously, and then more deeply to numb the skin and underlying tissues. Allow it to have its effect for 3–5 minutes.
- » **Insert the spinal needle:** Put the needle between the vertebrae (spinous processes) into the subarachnoid space aiming for the L3-L4 or L4-L5 interspace. Pass through the skin, subcutaneous tissue, supraspinous ligament and interspinous ligament, and then you will feel the 'cheese-like' resistance of the ligamentum flavum. A 'pop' may be felt when the dura is breached, and the needle is in the intrathecal space. CSF should drip freely from the needle on removing the introducer.
- » **Measure Pressure:** Use a special tool called a manometer to measure the pressure and record readings. Write down the highest number you see. (normal is ~6–20 cmH₂O)
- » **Collect cerebrospinal fluid (CSF)** into the collection tubes, noting the volume and characteristics.
 - ☞ Take four samples, for each of the four pots, and then another for one of the glucose bottles, roughly five drops in each. Send samples 1 and 3 for microscopy cell count and culture.
 - ☞ Send sample 2 to biochemistry for protein measurement and xanthochromia if indicated (requires an opaque container for the bottle). Store sample 4 in the fridge in case more tests are needed later.
- » **Remove the needle:** Remove the needle and press on the puncture site to prevent CSF leakage.

- **Wound Covering:** Cover the insertion site with a small sterile dressing to protect against infection.
- **Advice:** the patient lies flat for roughly 1 hour after the procedure.
- **Manage Headaches:** Explain post-LP headache and treat as needed with analgesia.
- **Patient Comfort:** Ensure the patient's comfort throughout the procedure.
- **Monitoring:** Monitor the patient for signs of distress or discomfort during the procedure. Provide reassurance and support as needed.
- **Gratitude:** Thank the patient for their cooperation.
- **Documentation:** Document the details of the procedure including the date, time of procedure, indication, fluid findings (pressure, amount, color, and consistency of the aspirated fluid) for accurate record-keeping and analysis purposes, post-procedure instructions, follow-up plan, and provider signature.
- **Waste Disposal:** Dispose of all used materials appropriately to maintain cleanliness and safety.



CAUSES OF DRY TAP

It means CSF does not come out through the LP needle, could be due to:

- Improper positioning of the needle, i.e. needle is not in the subarachnoid space. This is a common cause.
- Subarachnoid space is obliterated by a tumour or adhesive arachnoiditis.

INDICATION OF LUMBAR PUNCTURE

A. **Diagnostic:** CSF is removed for diagnosis of the following conditions:

- **CNS infections/inflammation:** Encephalitis, Meningitis, Multiple sclerosis, Myelitis
- Acute post-infective polyneuritis (Guillain-Barre syndrome)
- Subarachnoid haemorrhage (to be done after fundus examination)
- **Infiltrative conditions:** Lymphoma and leukaemic infiltration of meninges
- To confirm raised intracranial pressure when CT scan excludes the danger of brainstem herniation
 - Benign raised intracranial tension
 - Cerebral venous sinus thrombosis
- **Instillation of contrast media or an isotope**
 - Myelography (CT myelography)
 - Cisternography.

B. **Therapeutic**

Lumbar puncture is done for treatment purposes.

- 1) Administration of intrathecal antibiotics or tetanus immunoglobulin
- 2) Administration of antileukaemic drugs in ALL
- 3) Spinal anaesthesia
- 4) Removal of CSF to lower the pressure in benign intracranial hypertension.

C. **Other uses of LP needle:** Used as aspiration needle for tapping fluids from a cavity, e.g. ascites, pleural effusion.

CONTRAINDICATION OF LUMBAR PUNCTURE

- 1) Thrombocytopenia and coagulation disorders
- 2) Depressed consciousness especially if focal neurological signs are present. CT scan to be done initially to rule out raised intracranial pressure or mass lesion. LP should not be performed in the presence of raised intracranial pressure or a mass lesion.
- 3) Papilloedema Skin infection at the site of lumbar puncture. It is not a contraindication; LP can be done one space higher.
- 4) Lumbar meningocele

COMPLICATION OF LUMBAR PUNCTURE

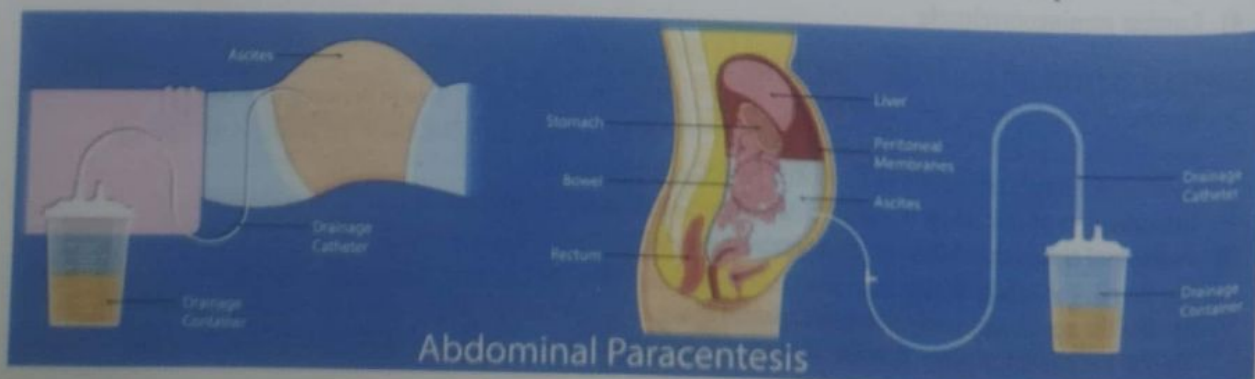
- **Brainstem herniation or cerebellar coning:** To avoid this LP should not be done in presence of gross papilloedema. In dire emergency, slow removal of CSF by keeping the stylet inside the needle is advised and signs of brainstem herniation to be looked for (change in size of pupil).
- **Introduction of infection:** To avoid it, aseptic precautions are to be followed.
- **Postspinal headache:** Measures to avoid/treat it are;
 - 1) Remove the fluid slowly.
 - 2) Put the needle obliquely into subarachnoid space.
 - 3) Put the patient in prone position if headache develops.

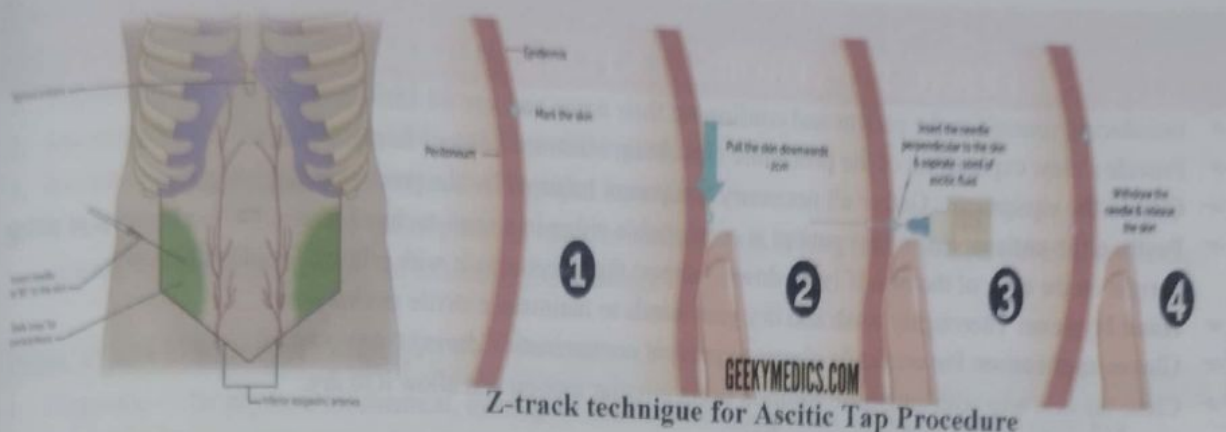
ASCITIC TAP (DIAGNOSTIC PARACENTESIS, PARACENTESIS ABDOMINIS)

- ☞ Introducing yourself to the patient and confirming their name and age for identification.
- ☞ Provide a clear explanation of the procedure and obtain informed consent from the patient.
- ☞ **Gather the equipment:** Gather all necessary equipment required for the procedure.

» Sterile gloves	» Antiseptic solution e.g. pyodine
» Sterile suction catheter	» Local anesthetics: Lidocaine 1% or 2%
» Sterile drapes and disposable under pads.	» Syringe for local anesthesia 25g.
» Paracentesis kit (needle/catheter)	» Specimen tubes
» Collecting bag and Sterile dressing	» Syringes (10ml or 20ml) for collection

- ☞ Practice hand hygiene and wear sterile gloves.
- ☞ Ensure the patient empties their urinary bladder before the procedure to enhance comfort.
- ☞ Place the patient comfortably in a semi-recumbent or sitting position with the abdomen exposed.
- ☞ **Establish IV Access:** start **Inj. Haemaccel 500ml x IV x STAT** to maintain the homeostasis.
- ☞ Perform an abdominal examination to confirm the presence of ascites (shifting dullness).
- ☞ **Local Anesthesia:** Administer local anesthesia at the puncture site to minimize discomfort.
- ☞ **Ultrasound (if available):** Ideally, ultrasound is used to confirm the presence of ascites and identify a suitable needle insertion site. However, it is possible to perform this procedure without ultrasound.
- ☞ **Needle Insertion procedure:**
 - » Clean the skin with antiseptic solution using circular motion and allow it to dry.
 - » Using sterile technique, drape the area and locate the puncture site, usually performed in the right or left lower quadrant of the abdomen, where the ascitic fluid accumulates most. Avoid performing the tap too superiorly, due to the risk of injuring the liver or spleen. Be cautious of the inferior epigastric artery located within the rectus sheath. Insert the paracentesis needle or a large 18-gauge cannula into the abdominal cavity, either under ultrasound guidance or using anatomical landmarks such as:
 - A. Midway between the symphysis pubis and umbilicus (after bladder evacuation).
 - B. Junction of the lateral 1/3rd and medial 2/3rd of the right or left spino-umbilical line.
- ☞ **COLLECTION OF ASCITIC FLUID:**
 - » Connect the needle to a rubber tubing to facilitate the slow drainage of ascitic fluid into a collecting bag or bottle monitoring for any signs of complications such as pain or bleeding.
 - » **Volume drained:** Typically, 1-2l of fluid may be drained over 4-6 hours in a single sitting. For liver cirrhosis, large volume paracentesis may be necessary, aspirating 3-5L of fluid in one session.
 - » **Albumin infusion:** Following large volume paracentesis in cirrhotic patients, administer 6-8 grams per liter of salt-free albumin infusion to prevent complications.
 - » **Diagnostic aspiration:** Collect ascitic fluid into specimen tubes for analysis, noting its volume and characteristics. For diagnostic purposes, aspirate approximately 20-50 ml of ascitic fluid.
- ☞ Remove the needle or catheter once an adequate amount of fluid has been drained.
- ☞ Apply pressure to the puncture site and cover with a sterile dressing to prevent leakage or infection.
- ☞ **Patient comfort:** Ensure the patient's comfort throughout the procedure.
- ☞ **Monitoring:** Monitor the patient for any signs of complications such as bleeding, infection, or hypotension post-procedure. Provide reassurance and support as needed.
- ☞ **Gratitude:** Thank the patient for their cooperation.
- ☞ **Documentation:** Record the details of the procedure, including date, time, location of the paracentesis, additionally the amount, color, and consistency of the aspirated fluid, for accurate record-keeping and analysis purposes and specify the indication for the procedure (e.g., ascites due to cirrhosis, malignancy).
- ☞ **Waste Disposal:** Dispose of all used materials appropriately to maintain cleanliness and safety.





Z-track technique for Ascitic Tap Procedure

Z-TRACK TECHNIQUE

- It is an alternative method to prevent ascitic fluid leakage after paracentesis.
 - » Stretch the skin about 2cm before inserting the needle.
 - » Keep the skin stretched while advancing the needle.
 - » Release the skin after removing the needle.
- This technique creates a non-linear path (zigzag path) between the skin and abdominal cavity.

CAUSES OF DRY TAP

Failure to obtain ascitic fluid on attempted aspiration may be due to

1. Needle blockade by omental patch.
2. Perforation of a viscus.
3. Presence of very little fluid which could not be targeted blindly.

INDICATION OF ASCITIC TAPPING

They are divided into diagnostic and therapeutic indications:

1. Diagnostic paracentesis (e.g., cirrhosis, tuberculous or malignant ascites).
 2. Severe abdominal discomfort or cardio-respiratory embarrassment. *
 3. Refractory to medical therapy. *
 4. Danger of strangulation of umbilical hernia, if present. *
 5. Paracentesis may allow better abdominal examination, needle biopsy of liver, scanning or ultrasonography. *
- ❖ *2, 3, 4 and 5 are therapeutic indications.

CONTRAINDICATION ASCITIC TAPPING

1. Infection overlying the intended needle insertion site. if present, choose alternative site on the abdomen
2. Cirrhosis of liver in hepatic pre-coma.
3. Bleeding diathesis: Coagulopathy (INR >2.0), Platelets <50
4. Acute abdomen.
5. Pregnancy
6. Organomegaly

COMPLICATION ASCITIC TAPPING

1. Sudden cardio-respiratory distress or shock (if appears during the paracentesis, urgently stop tapping the fluid).
2. Introduction of infection (peritonitis).
3. Precipitation of hepatic coma (the compressed porto-caval shunts open up and nitrogenous materials reach the brain by-passing the liver).
4. Perforation of hollow viscus (bladder or bowel).
5. Protein depletion (5 litre of ascitic fluid may contain 50-100 g of protein).
6. Constant oozing of fluid (especially intense ascites or malignant ascites).

N.B.: Peritoneal biopsy is done with Cope's needle in a suspected case of tuberculous or malignant ascites, or ascites of uncertain origin.

PLEURAL TAP (THORACENTESIS/THORACOCENTESIS)

- 
- ☞ Introducing yourself to the patient and confirming their name and age for identification.
 - ☞ Provide a clear explanation of the procedure and obtain informed consent from the patient.
 - ☞ **Gather the equipment:** Gather all necessary equipment required for the procedure.
 - ☞ **Position the patient:** Ensure the patient is comfortable either in a semi-reclined position with a backrest or sitting upright on the edge of the bed. If lying down, support the affected side with pillows for added comfort.
 - ☞ **Hand Hygiene:** Thoroughly wash and dry your hands to maintain a sterile environment.
 - ☞ **Gloves application:** Put on sterile gloves to prevent contamination during the procedure.
 - ☞ Clean the skin area with antiseptic solution using circular motion and allow it to dry.
 - ☞ **Locations: the site of aspiration may be:**
 1. 6th intercostal space (ICS) in the midaxillary line,
 2. 7th ICS in the posterior axillary line, or
 3. 8th ICS in the Scapular Line.
 4. Loculated or encysted effusion — area of maximum dullness is the site of puncture (may require USG-guidance for actual localization).
 - ☞ **Needle Insertion:**
 1. Locate the puncture site, typically in the mid-axillary line just below the rib margin.
 2. Insert the needle into the pleural space using a steady hand and sterile technique.
 3. Numb the aspiration site with 2% lignocaine solution, infiltrating from the skin up to the parietal pleura through the subcutaneous tissue.
 4. Insert the pleural aspiration needle vertically above the upper border of the lower rib to avoid nerve and vessel injury, piercing the parietal pleura until a 'give away' sensation is felt.
 5. Attach the needle to a three-way cannula and then connect the cannula to a 50 ml syringe.
 6. Apply suction to the syringe to draw pleural fluid into it, which is then expelled into a kidney-tray via the cannula outlet by adjusting its screw.
 - ☞ **Collection of fluid:**
 1. Aspirate fluid slowly, stopping before it becomes harmful to the patient (therapeutic aspiration).
 2. Some clinicians suggest not aspirating more than 1 liter of pleural fluid initially to avoid acute pulmonary edema. Repeat aspiration may be considered after 3–4 days, following a check X-ray to assess remaining fluid or lung expansion.
 3. If the patient experiences coughing, respiratory distress, chest tightness, or severe restlessness, stop the aspiration immediately.
 4. Remove the needle or catheter once an adequate amount of fluid has been drained.
 5. Apply pressure to the puncture site and cover with a sterile dressing to prevent leakage or infection.
 6. Cover the insertion site with a small sterile dressing to protect against infection.
 - ☞ **Fluid analysis:** Label the collected fluid samples appropriately for analysis. Send samples for laboratory testing, including cell count, protein, glucose, pH, and microbiological culture.
 - ☞ **Patient comfort:** Ensure the patient's comfort throughout the procedure.
 - ☞ **Monitoring:** Monitor the patient for signs of distress or discomfort during the procedure. Provide reassurance and support as needed. The patient should be monitored for next 24 – 48 hours for development of any complication such as pneumothorax or bleeding.
 - ☞ **Gratitude:** Thank the patient for their cooperation.
 - ☞ **Documentation:** Document the details of the procedure including the date, time of procedure, indication, fluid findings (pressure, amount, color, and consistency of the aspirated fluid) for accurate record-keeping and analysis purposes. Note any complications and patient response, post-procedure instructions, follow-up plan, and provider signature.
 - ☞ **Waste Disposal:** Dispose of all used materials appropriately to maintain cleanliness and safety.

CAUSES OF DRY TAP

Failure to obtain pleural fluid on attempted aspiration may be due to

1. Empyema thoracis having very thick pus.
2. Encysted pleural effusion (needs USG- or CT-guided aspiration).
3. Interlobar or subpulmonic effusion (needs CT-guided aspiration).
4. A case of thickened pleura, tumour of pleura or massive consolidation of lung rather than pleural effusion (X-ray picture and clinical features may be misleading/simulating).

INDICATION PLEURAL TAPPING

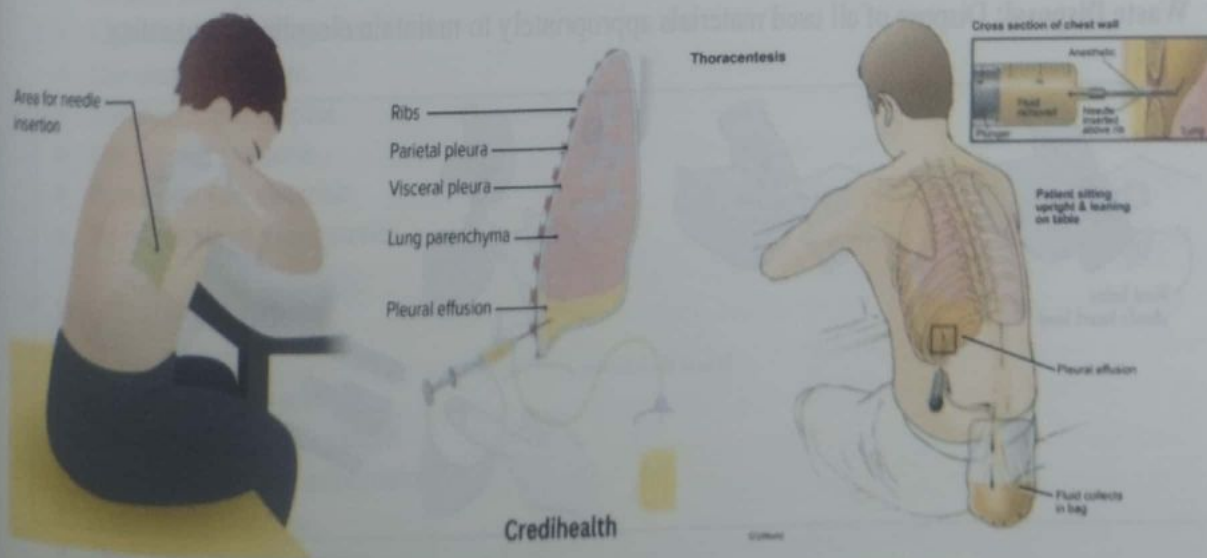
1. Diagnostic — for physical, biochemical, cytological and bacteriological study of pleural fluid to come to a definitive diagnosis. Approximately, 20-50 ml of fluid should be aspirated.
 2. Therapeutic — If there is,
 - » Respiratory distress,
 - » Massive collection,
 - » Rapid collection, and
 - » Suspected secondary infection of effusion.
- * * Instillation of drugs (cytotoxics, tetracycline) are done in malignant pleural effusion.

CONTRAINDICATION OF PLEURAL TAPPING

1. Coagulation disorder, platelet abnormality.
2. Patient with severe cough or hiccough.

COMPLICATION OF PLEURAL TAPPING

1. Pleural shock (as a result of vagal inhibition).
2. Empyema thoroacis.
3. Hydropneumothorax (iatrogenic).
4. Acute pulmonary oedema (non-cardiogenic) – If the fluid is aspirated very rapidly; unilateral.
5. Air embolism.
6. Injury to intercostal vessels and nerves.
7. Haemothorax.
8. Cardio-respiratory embarrassment with circulatory collapse.
9. Subcutaneous emphysema.
10. Late complication (rare) - Intercostal artery aneurysm.

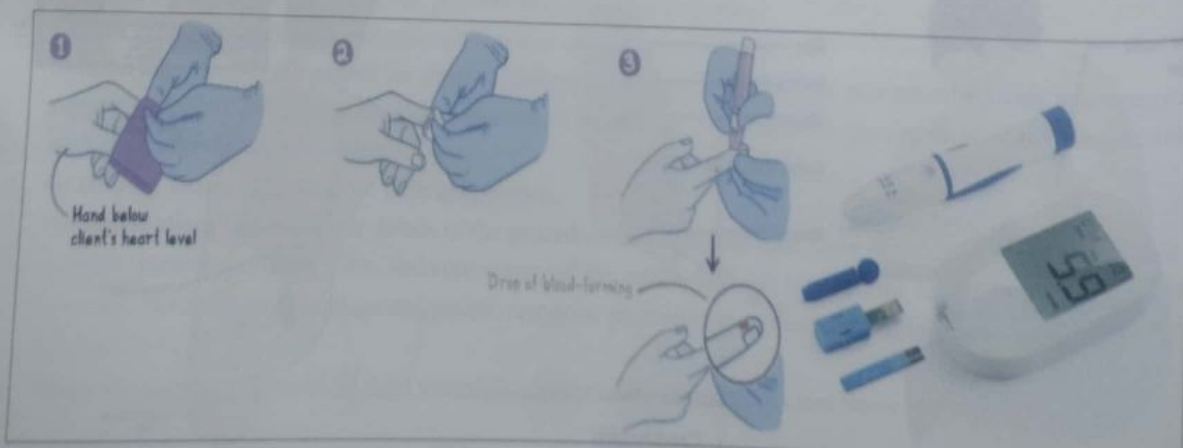


BEDSIDE BLOOD GLUCOSE MEASUREMENT

- ☞ Introducing yourself to the patient and confirming their name and age for identification.
- ☞ Provide a clear explanation of the procedure and obtain informed consent from the patient.
- ☞ **Gather the Equipment:** Gather all necessary equipment required for the procedure.

» A pair of non-sterile gloves	» A glucose monitor (Glucometer)
» An alcohol wipe.	» A spring-loaded pricker
» Cotton wool	» A lancet
» Test strips	» Insulin syringe

- ☞ **Hand Hygiene:** Thoroughly wash and dry your hands to maintain a sterile environment.
- ☞ **Gloves application:** Put on sterile gloves to prevent contamination during the procedure.
- ☞ **Prepare Equipment:** Insert a test strip into the glucometer and turn it on. Load the lancet into the pricker and prick the side of the finger. (It is less painful to prick the side rather than the tip of a finger because there are comparatively fewer nerve endings there)
- ☞ Massage the finger from its base to its tip to increase its perfusion.
- ☞ **Cleanse Site:** Cleanse the fingertip with an alcohol swab and allow it to dry completely.
- ☞ **Prick Finger:** Use a lancet device to prick the side of the fingertip for a blood drop.
- ☞ **Collect Blood:** Squeeze the finger to obtain a droplet of blood. Place the blood drop onto the designated area of the test strip. If no or insufficient blood is obtained, prick the finger again and be sympathetic to the patient's plight!
- ☞ **Read Results:** Wait for the glucometer to display the blood glucose level.
- ☞ **Provide Education:** Explain the significance of the blood glucose level and any necessary actions or interventions.
- ☞ Give the patient some cotton wool to stop any bleeding.
- ☞ **Patient Comfort:** Ensure the patient's comfort throughout the procedure.
- ☞ **Gratitude:** Thank the patient for their cooperation.
- ☞ **Wash Hands:** Thoroughly wash hands after completing the procedure to maintain hygiene.
- ☞ **Documentation:** Document the details of the procedure including the time, date, and record the blood glucose reading; random blood sugar (RBS) or fasting blood sugar (FBS) in patient blood sugar chart.
- ☞ **Waste Disposal:** Dispose of all used materials appropriately to maintain cleanliness and safety.





EXPLAINING CLINICAL SKILLS

- ☛ **Introduction:** Explaining clinical skills means describing the techniques and knowledge needed for good patient care. This involves understanding how to perform medical procedures, making accurate diagnoses, understanding test results (interpret tests), communicate well with patients and colleagues, and maintain professional ethics.
- ☛ **Patient education & Counseling for procedural skills**
 1. **Introduction:** Emphasize the role of patient education and counseling in preparing for medical procedures.
 2. **Identify Procedures:** Specify the procedural skills to be explained, such as endoscopy and needle aspiration.
 3. **Build trust:** Establish a connection with the patient to encourage open communication and trust.
 4. **Confirm patient understanding:** Check the patient's current understanding and if they're ready to learn more about the procedure.
 5. **Explain Purpose:** Clearly state why the procedure is necessary and how it can benefit the patient.
 6. **Address Concerns:** Encourage the patient to express any fears or concerns they may have about the procedure.
 7. **Describe Procedure:** Use simple language to explain each step of the procedure clearly and understandably.
 8. **Visual Aids:** Use pictures or models to show how the procedure works.
 9. **Demonstration:** Show how the procedure works using teaching tools, props or videos.
 10. **Answer Questions:** Allow ample time for the patient to ask questions and address any misconceptions.
 11. **Informed Consent:** make sure the patient fully understands the risks, benefits, and alternatives of the procedure before providing consent.
 12. **Provide emotional support and reassurance** throughout the education and counseling process.
 13. **Follow-Up:** Provide resources for more information and schedule follow-up appointments.
 14. **Gratitude:** Thank the patient for their cooperation.
 15. **Documentation:** Document the patient education and counseling session in the medical record, including any questions asked and answered.



☛ HOW TO DO IT:

- » Show empathy.
- » Listen to the patient's feelings.
- » Start with key information.
- » Be clear and specific.
- » Check understanding often.
- » Use simple language.
- » Use diagrams if helpful.
- » Use props if available.
- » Provide written materials.
- » Be honest about uncertainties.

☛ WHAT NOT TO DO:

- » Don't rush/hurry.
- » Don't reassure too soon.
- » Don't talk down to the patient.
- » Don't give too much information.
- » Avoid medical jargon.
- » Don't make up information.

PATIENT COUNSELLING FOR ENDOSCOPIC PROCEDURE

1. Introducing yourself to the patient and confirming their name and age for identification.
2. State the test required and its indication, e.g. "To help ascertain the cause of your bleeding, we would like to look at the inside of your stomach with a small telescopic camera."
3. Check the patient's current understanding, e.g. "Have you ever had this done before?"
4. Explain what the test involves (see below).
5. Highlight any special preparation involved, e.g. fasting for a certain period prior to the test.
6. Check the patient's understanding.
7. Ask whether he has any questions or concerns.
8. If possible, tell him where and when the test will take place.
9. If possible, give him a leaflet.
10. **Gratitude:** Thank the patient for their cooperation.
11. **Documentation:** Document the counseling session in the patient's medical record, including details of the discussion, any questions asked, and the patient's consent for the procedure.

Upper endoscopy (Oesophagogastroduodenoscopy = OGD, Gastroscopy)

PATIENT COUNSELING

- ☞ Upper endoscopy, also known as esophagogastroduodenoscopy (EGD), is a medical procedure that allows your doctor to examine the lining of your esophagus, stomach, and the first part of your small intestine.
- ☞ During the procedure, a thin, flexible tube called an endoscope is inserted through your mouth and down your throat into the stomach. IV sedation will be administered to ensure your comfort and minimize discomfort. In addition, your throat may be numbed with a local anaesthetic. The procedure itself usually takes about 15-20 minutes and is very safe. The endoscope has a small camera at the tip that sends images to a monitor, allowing your doctor to see the internal structures of your upper digestive organs.
- ☞ This procedure is typically performed to investigate symptoms such as difficulty swallowing, abdominal pain, heartburn, or gastrointestinal bleeding. It can help diagnose conditions such as cancer, inflammation, infection, tumors, or abnormal growths. Additionally, it permits the collection of tissue samples (biopsies) for further examination and even to stretch the gullet or stop bleeding.
- ☞ **Before the procedure, you will receive instructions for fasting and** you should not eat or drink anything for at least four hours. If you are on any prescribed medicines for indigestion, you should stop taking them for at least two weeks (this does not also apply to antacids). After the procedure, you will be taken to a recovery room where you can remain until the effects of the sedation have worn off. Once the diagnosis is complete, your doctor will discuss the findings with you and may provide further treatment or follow-up care as needed.

FURTHER KNOWLEDGE FOR DOCTORS

- ☞ Upper endoscopy is used to look for lesions in the oesophagus, stomach, or duodenum. It can also be used to take biopsies and perform therapeutic and palliative interventions e.g. repair bleeding ulcers or veins, dilate the oesophagus, remove polyps and early-stage tumours, or provide nutrients.
- ☞ **Common indications** include dysphagia, dyspepsia, haematemesis, melaena, malabsorption, persistent abdominal pain, and unexplained weight loss.
- ☞ **Complications** include pain, bleeding, perforation, infection, sore throat, and aspiration.

LOWER ENDOSCOPY (COLONOSCOPY OR SIGMOIDOSCOPY)

PATIENT COUNSELING

- ☛ Colonoscopy involves passing a thin, flexible tube or scope through the back passage and into the colon or large bowel. IV sedation will be administered to ensure your comfort and minimize discomfort.
- ☛ Additionally, the area may be numbed with a local anesthetic. The procedure typically takes about 20-30 minutes and is considered very safe.
- ☛ After performing a digital rectal examination, the operator will gently push the scope through the back passage and into the colon. Air will be passed up a channel in the scope to make the colon easier to visualize. This may make you feel cramped or bloated, which is normal.
- ☛ The endoscope has a small camera at the tip that sends images to a monitor, allowing your doctor to see the internal structures of your lower digestive tract.
- ☛ This procedure is typically performed to investigate symptoms such as rectal bleeding, changes in bowel habits, or abdominal pain. It can help diagnose conditions such as polyps, inflammation, diverticulosis, or colorectal cancer. Collection of tissue samples (biopsies) may also be taken during the procedure for further examination, and certain therapeutic interventions, such as polyp removal, can be performed and even to remove small lumps of tissue or stop bleeding.
- ☛ Before the procedure, you will receive instructions for bowel preparation, which may involve dietary restrictions and medication adjustments. You should refrain from eating or drinking anything for a specific period before the procedure, and certain medications may need to be stopped temporarily. The colon needs to be empty for the procedure, and you will have to go on a special diet for the few days leading up to the test. You will also be given some laxatives to take. After the procedure, you will be taken to a recovery room where you can remain until the effects of the sedation have worn off. Once the diagnosis is complete, your doctor will discuss the findings with you and may provide further treatment or follow-up care as needed.



FURTHER KNOWLEDGE FOR DOCTORS

- ☛ Colonoscopy is used to look for pathology in the colon as far as the terminal ileum. It enables the operator to take biopsies and perform therapeutic and palliative interventions, e.g. remove polyps, stop bleeding, insert a stent. It is also used for surveillance in those at risk of colorectal cancer or patients with IBD.
- ☛ **Common indications** for colonoscopy include PR bleeding, positive faecal occult blood test, persistent lower abdominal pain, persistent diarrhoea, and change in bowel habit.
- ☛ **Complications** include pain, bleeding, perforation, and infection.
- ☛ **Flexible sigmoidoscopy** is used to look at the rectum and lower colon (up to about 60 cm), sometimes as precursor to a full colonoscopy. The procedures are similar.



OBTAINING MEDICAL CONSENT

- ☞ Introducing yourself to the patient and confirming their name and age for identification.
- ☞ **Explanation of Procedure or Treatment:** Clearly explain the proposed procedure or treatment, including its purpose, risks, benefits, alternatives, and potential complications.
- ☞ **Patient perception:** Ensure that the patient comprehends the information provided by allowing them to ask questions and addressing any concerns they may have.
- ☞ **Voluntariness:** Confirm that the patient is providing consent voluntarily without any coercion or undue influence.
- ☞ **Capacity to consent:** Assess the patient's capacity to provide consent, ensuring they are mentally competent to make informed decisions about their healthcare.
- ☞ **Consent for specific procedures:** Obtain consent specifically for the procedure or treatment being performed, clearly specifying what the patient agrees to.
- ☞ **Consent for medical photography or Recording:** If applicable, obtain separate consent for any medical photography, video recording, or audio recording that will be conducted during the procedure or treatment.
- ☞ **Consent for anesthesia or Sedation:** If anesthesia or sedation is administered, ensure that the patient understands and consents to this aspect of the procedure.
- ☞ **Consent for student or observer participation:** If medical students or observers will be present during the procedure, obtain separate consent from the patient for their participation.
- ☞ **Documentation:** Record the details of the consent process in the medical notes, including the information provided to the patient, any questions asked, or concerns raised, and the patient's agreement to proceed with the procedure or treatment.

THE PURPOSE OF GAINING CONSENT:

- ☞ Consent ensures that patients are informed about their healthcare options, including proposed procedures, treatments, or interventions, along with their associated risks, benefits, alternatives, and potential complications.
- ☞ Consent empowers patients to make informed choices about their own healthcare, respecting their right to self-determination and bodily autonomy (control over your own body/your body your rules). Consent builds trust between patients and healthcare providers, encouraging collaboration in decision-making based on mutual respect and shared decision-making.

HOW LONG IS CONSENT VALID FOR:

- ☞ The validity of consent depends on various factors, including the nature of the procedure or treatment, changes in the patient's condition or circumstances, and any new information that may impact the patient's decision-making process.
- ☞ In general, consent is considered valid for the duration of the specific procedure or treatment being performed. However, if there are significant changes in the patient's condition or if additional interventions are proposed, healthcare providers should reassess consent and ensure that patients are adequately informed before proceeding.

REFUSAL OF TREATMENT:

- ☞ Patients have the right to refuse any proposed treatment or intervention, provided they have the capacity to make informed decisions about their healthcare. Healthcare providers should respect patients' autonomy and decision-making authority, even if they disagree with the patient's choice.
- ☞ When a patient refuses treatment, healthcare providers should engage in open and respectful communication, exploring the reasons behind the refusal, addressing any concerns or misconceptions, and offering alternative options or supportive care as appropriate. It's essential to document the patient's refusal of treatment.
- ☞ Competent adult patients are entitled to refuse treatment even when doing so may result in permanent physical injury or death. For example, if a religious person, or a person of faith, may refuse a blood transfusion even if it means certain death. An adult patient is considered competent if they can:
 - Understand what's being suggested.
 - Know why it's being suggested.
 - Learn about other options, including doing nothing.

- Recognize the good and bad points of the suggestion and its alternatives.
- Understand the possible outcomes.
- Remember the information long enough to make a thoughtful decision, even if they can't make one.

PATIENT'S CHOICE: UNDERSTANDING CONSENT

- When seeking consent, avoid just going through a checklist. Instead, talk with the patient to understand their thoughts, concerns, and expectations, and adjust your explanations accordingly.
 1. Provide information about the intervention, using diagrams if helpful.
 2. Explain why the intervention is recommended.
 3. Discuss alternative options, including the choice of not proceeding with the intervention.
 4. Describe the main benefits and risks of intervention and its alternatives.
 5. Outline the potential consequences of both the intervention and its alternatives.
- Ask the patient to repeat what you've explained and make sure they're able to agree.
- Remind the patient that they are not obligated to make an immediate decision and that they can change their mind at any time.

CONSENT FOR OPEN APPENDICITOMY AS EXAMPLE

We have been informed about the patient's condition, which reveals appendicitis in the lower part of the abdomen, which requires treatment through surgery. During this operation, the patient will be completely unconscious, and possible complications may include cardiac arrest, heart attack, or damage to the intestines leading to blood clotting in the legs and stroke.

The possible complications during the operation are as follows:

1. Significant blood loss may occur during the operation, which may require the need for a blood transfusion.
2. Any organ in the patient's abdomen may be damaged during the operation, and there is also a risk of cutting a blood vessel.
3. It is also possible that upon operating, it is discovered that the problem is not with the appendix but with the intestine. In this case, the affected intestine may be removed and, depending on the situation, the intestine may need to be pulled out through the abdomen by making an opening and placing a bag, known as a stoma bag or colostomy bag.
4. The patient may also experience infection and pain after the operation, and in case of wound breakdown, a drain may need to be placed in the wound.

We have been informed about the complications of this operation, and in the event of any complication, the doctors or hospital staff will not be responsible. Understanding the complexities of this operation, we grant permission for the surgery.

Patient's Name:	Patient's Signature:
Name of Relative and Relationship to Patient:	Relative's Signature:
Relative's ID Card Number:	Emergency mobile No:

ہمیں بتایا گیا ہے کہ مریض کا پیٹ درد اسی وجہ سے ہے کہ پیٹ کے نچلے حصے میں اینڈیکس کی سوزش ہو گئی ہے، جس کا علاج آپریشن کے ذریعے کیا جاتا ہے۔ اس آپریشن کے دوران مریض کو مکمل طور پر بے ہوش کیا جائے گا، اور اس کے ممکنہ پیچیدگیوں میں دل کا رکتا، دل کا دورہ پڑنا، یا آنتوں کو نقصان ہونا، ٹانگوں میں خون جمنا اور فالج شامل ہیں۔

- آپریشن کے دوران آنے والی ممکنہ پیچیدگیوں مندرجہ ذیل ہیں:
- 1- آپریشن کے دوران مریض کا بہت زیادہ خون کا ضیاع ہو سکتا ہے۔ جسکی وجہ سے خون کی ضرورت بھی پڑ سکتی ہے۔
 - 2- آپریشن کے دوران مریض کے پیٹ میں کسی بھی عضو کو نقصان پہنچ سکتا ہے، اور رگ کاٹنے کا خطرہ بھی ہوتا ہے۔
 - 3- ممکن ہے کہ آپریشن کرنے کے دوران پتہ چلے کہ مسئلہ اینڈیکس میں نہیں ہے بلکہ آنتھ کا ہے۔ اس صورت میں پیٹ کے درمیان چیرا دے زخمی آنتھ کو کاٹا جا سکتا ہے، اور مواد کو باہر نکالنے کے لیے پیٹ کے رستے پر ایک بیگ لگایا جا سکتا ہے، جسے سٹوما بیگ یا کولوسٹومی بیگ کہتے ہیں۔
 - 4- آپریشن کے بعد مریض کو انفیکشن اور درد کی شکایت بھی ہو سکتی ہے، اور زخم کا ٹوٹنا ہونے کی صورت میں زخم میں ایک پمپ لگایا جا سکتا ہے۔

ہمیں اس آپریشن کی پیچیدگیوں کے بارے میں معلومات فراہم کی گئی ہیں، اور کسی بھی پیچیدگی کی صورت میں ڈاکٹر یا ہسپتال کے عملہ ذمہ دار نہیں ہوں گے۔ اس آپریشن کی پیچیدگیوں کو سمجھتے ہوئے، ہم آپریشن کی اجازت دیتے ہیں۔

مریض کے دستخط:	رشتہ دار کا نام اور مریض سے رشتہ:
رشتہ دار کے دستخط:	رشتہ دار کا شناختی کارڈ نمبر:
ایمرجنسی موبائل نمبر:	

BREAKING BAD NEWS & DISCUSSING GOALS OF CARE

Breaking bad news is a sensitive process requiring empathy and clear communication. The following basic approach is not comprehensive but should help you get started and to help navigate this challenging task.

- ☛ **Introduce yourself and choose the right setting:** Select a private and comfortable environment where the patient feels safe and supported. Ensure there are no distractions or interruptions. Confirm who should be present, allocate sufficient time, and choose a quiet, private space.
- ☛ **Breaking Bad News:** Follow a structured protocol like SPIKES (Explained below). Use clear and simple language to deliver the news gradually, allowing time for processing and questions.
- ☛ **Goals of Care:** Discussing goals of care involves understanding the patient's wishes and preferences. This may include decisions about life-saving measures, end-of-life care, and treatment options.
- ☛ **Use Ask-Tell-Ask:** Employ a cycle of asking, telling, and re-asking to ensure understanding and address concerns throughout the conversation.
 - » **Ask:** Find out what the patient or family member's baseline understanding of the current clinical situation is.
 - » **Tell:** Give information in small "chunks," with pauses in between to allow for processing and questions.
 - » **Ask:** Periodically check for understanding.
- ☛ **Preparation:** Before delivering the bad news, prepare yourself mentally and emotionally. Anticipate the patient's reaction and plan what you will say.
- ☛ **Start with Empathy:** Begin the conversation by expressing empathy and compassion. Acknowledge the seriousness of the situation and convey your willingness to support the patient through it.
- ☛ **Use Clear and simple language:** Deliver the news in clear, straightforward language that the patient can understand. Avoid medical jargon and euphemisms.
- ☛ **Break the news gradually:** Avoid delivering the bad news all at once. Instead, break it down into smaller, more digestible pieces. Give the patient time to process each piece of information before moving on.
- ☛ **Allow emotional expression:** Encourage the patient to express their emotions freely. Listen attentively and validate their feelings without judgment.
- ☛ **Provide Information:** Offer relevant information about the diagnosis, prognosis, and available treatment options. Be honest and transparent but avoid overwhelming the patient with too much information at once.
- ☛ **Offer Support:** Reassure the patient that they are not alone and that you will support them throughout their journey. Provide resources for additional support, such as counseling services or support groups.
- ☛ **Respect Autonomy:** Respect the patient's autonomy and involving the patient in decisions about their care while providing guidance & support. Their choices should be respected & honored throughout the process.
- ☛ **Follow-Up:** Schedule a follow-up appointment to families discusses next steps and address any further questions or concerns the patient may have. Offer ongoing support and reassurance as needed.

Helpful phrases for conversations involving breaking bad news and goals of care

"I'm sorry."	"I wish things were different," or "I wish there was a way we could cure your illness."
"There's nothing more we can do."	"Let's talk about what we can do from here."
"We need to talk about your goals of care."	"I know these things can be tough to talk about, and I like to hope for the best, but prepare for the worst. Is it ok if we talk about what your preferences might be if things were to get worse?"
"Do you want everything to be done?"	Step 1: Ask the patient about their goals and values. For example: "What's most important to you?" "What do you hope for?" "What are you most worried about?" "What makes life worth living for you?" "Do you have a source of spiritual support?" Step 2: Ask the patient about their understanding of medical terms such as: CPR, DNR and DNI orders, hospice CARE (focuses on the care, comfort, & quality of life), palliative care etc. Clarify and explain as necessary, in patient-friendly language. Step 3: Ask the patient for their preferences. For example: "Have you thought about what kinds of treatment you might want if you were to die suddenly (meaning your heart or your breathing stopped)?" "Have you thought about who you might like to make decisions for you if you weren't able to make them for yourself?"

DNR = do not resuscitate, DNI = do not intubate, CPR = Cardiopulmonary resuscitation

END-OF-LIFE COUNSELING

• **End-of-life counseling** is a caring and personalized approach that helps people nearing the end of their life. It focuses on practical, emotional, and spiritual needs, aiming to support both patients and their families. The goal is to encourage open conversations, shared decision-making, and overall well-being during this challenging time.

• THE GOALS OF END-OF-LIFE COUNSELING INCLUDE:

1. **Empowering Patient Involvement:** Engage the patient in end-of-life treatment decisions to enhance care, comfort, and quality of life, ensuring their preferences and values are respected.
2. **Supporting Open conversation:** Encourage honest and open discussions about the patient's wishes, fears, and concerns regarding end-of-life care, allowing them to express their preferences and values.
3. **Emotional Support:** Offer psychosocial support, empathy, and comfort to both the patient and their family or caregivers, acknowledging the emotional challenges associated with terminal illness and loss.
4. **Honoring Patient Wishes:** Respect and uphold the patient's preferences for care and involvement of others, promoting autonomy and dignity. Collaborate with patients to establish and rank their goals for end-of-life care, considering their values, preferences, and quality-of-life factors.
5. **Promoting Understanding:** Help patients and families understand their diagnosis, prognosis, and available treatment options, empowering them to make informed decisions about their care.
6. **Facilitating Advance Care Planning:** Assist patients in completing advance directives, such as living wills and durable power of attorney for healthcare, to ensure their wishes regarding medical treatment are honored in the event they become unable to communicate.
7. **Addressing Spiritual and Existential Needs:** Provide support and guidance in exploring spiritual and existential concerns, helping patients find meaning, purpose, and comfort as they approach the end of life.
8. **Supporting Family Dynamics:** Acknowledge and address the unique dynamics and relationships within the patient's family, helping them navigate difficult conversations and decisions together.
9. **Ensuring Comfort and Dignity:** Advocate for measures to manage symptoms, alleviate pain, and enhance quality of life, promoting comfort, dignity, and a peaceful end-of-life experience.
10. **Informing Care Team:** Ensure that all individuals involved in the patient's care, including healthcare professionals and support staff, are informed of the patient's preferences and family's wishes regarding end-of-life treatment and palliative care.

• **SPIKES PROTOCOL:** Recommended guidelines which help doctors deliver bad news to patients.

1. **Setting up the interview:** Begin by preparing yourself and the environment. Ensure privacy and adequate time for the conversation. Introduce yourself and clarify the purpose of the meeting.
2. **Assessment of the patient's perception:** Ask the patient what they understand about their condition and prognosis. This helps gauge their level of understanding and provides a starting point for the discussion.
3. **Inviting information from the patient:** Allow the patient to express their thoughts, feelings, and concerns. Encourage them to share as much or as little as they feel comfortable with. Use open-ended questions to explore their emotions and understanding.
4. **Giving knowledge and information to the patient:** Provide clear and honest information about the patient's condition, prognosis, and available treatment options. Use simple language and avoid medical jargon. Offer information gradually, allowing the patient time to process and ask questions.
5. **Addressing emotions with empathetic responses:** Acknowledge and validate the patient's emotions. Express empathy and compassion, and actively listen to their concerns. Offer support and reassurance and be sensitive to cultural and spiritual beliefs.
6. **Strategy and summary:** Collaborate with the patient to develop a plan moving forward. Discuss goals of care, treatment options, and preferences for end-of-life care. Summarize the key points of the discussion and ensure the patient understands the information provided.



COUNSELING FOR TERMINALLY ILL PATIENTS

Counseling for terminally ill patients involves a comprehensive approach aimed at providing emotional support, addressing spiritual needs, facilitating family reconciliation, and promoting physical comfort. Here's a stepwise guide on how counselors can prepare a client with a terminal illness to face death:

1. **Establishing Rapport and Trust:**
 - » Introduce yourself and explain your role in the patient's care.
 - » Create a safe and comfortable environment for open discussion.
2. **Assessing Understanding:**
 - » Gauge the client's comprehension of their illness and prognosis.
 - » Assess their emotional state and readiness to discuss end-of-life matters.
3. **Providing Information:**
 - » Use clear, empathetic language to explain the diagnosis, prognosis, and treatment options.
 - » Discuss goals of care, including symptom management and palliative care.
4. **Encouraging Expression of Concerns:**
 - » Encourage the client to share fears, worries, and goals for the future.
 - » Validate their emotions and provide empathetic responses.
5. **Exploring Values and Preferences:**
 - » Discuss the client's values, preferences, and priorities regarding their care and end-of-life wishes.
 - » Explore preferences for pain management, life-sustaining treatments, and advance directives.
6. **Facilitating Decision-Making:**
 - » Support the client in making informed decisions about their care and treatment options.
 - » Respect their autonomy and honor their choices.
7. **Addressing Spiritual Needs:**
 - » Explore the client's spiritual beliefs and concerns about death and the afterlife.
 - » Offer spiritual support and guidance based on the client's individual beliefs.
8. **Supporting Emotional Coping:**
 - » Provide emotional support and validation of the client's feelings throughout the counseling process.
 - » Teach coping mechanisms to help manage anxiety, fear, and grief.
9. **Navigating the Kübler-Ross Model:** Discuss the stages of grief outlined by Kübler-Ross (denial, anger, bargaining, depression, acceptance) and how they may manifest in the client. Recognize that grief is unique to each individual and may not follow a linear progression.
 - » **Stage 1: Denial** – At first the reaction is "No! Not me!" Most people find it hard to believe how sick they are even though they don't fully deny it.
 - » **Stage 2: Anger** – The patient feels angry/upset with everyone and everything around them. They might blame high healthcare costs or even the doctors for their situation.
 - » **Stage 3: Bargaining** – The patient tries to "make agreements" with God or other people to try to live longer.
 - » **Stage 4: Depression** – The patient feels very sad, hopeless, and starts to pull away from others as they realize they're going to die soon.
 - » **Stage 5: Acceptance** – In this final step, the person comes to accept death, feeling ready to face it, even though not necessarily with happiness.
10. **Promoting Social Support:**
 - » Facilitate family therapy sessions to address unresolved conflicts and promote reconciliation.
 - » Encourage meaningful social interactions and rituals that provide comfort and support.
11. **Ensuring Physical Comfort:**
 - » Address pain management and provide education on pain relief techniques.
 - » Empower the client to advocate for their physical comfort and well-being.
12. **Creating Meaningful Memories:**
 - » Help the client and their loved ones create meaningful experiences and memories together.
 - » Support storytelling, reminiscing, and legacy-building activities.
13. **Facilitating Family Reconciliation:**
 - » Assist in resolving family conflicts and fostering open communication among family members.
 - » Provide support for families to address unfinished business and express love and forgiveness.
14. **Continuing Support and Bereavement Care:**
 - » Offer ongoing counseling and support to the client and their family during the end-of-life journey.
 - » Provide bereavement support for family members after the client's passing.

DEATH CONFIRMATION & DEATH CERTIFICATION

DEATH CONFIRMATION

- **Death Confirmation** is the process of verifying that an individual has passed away, typically conducted by a healthcare professional (physicians or trained nurse) or a qualified authority. It involves assessing vital signs and clinical criteria to establish that life has ceased.
- **Confirmation by Physician:** Have a qualified physician confirm cessation of life.
- **Observation Period:** The patient should be observed for at least 5 minutes.
- **Assessment of Vital Signs:** Check for absence of pulse, heartbeat, and breathing.
- **General Appearance:** Note the absence of respiratory movements and absence of breath sounds.
- **Stimulus Response:** Confirm the patient does not respond to verbal or tactile stimuli (pressure on a nailbed).
- **Pupillary Response to light:** Check for fixed and dilated pupils.
- **Reflex Assessment:** Assess absence of corneal reflexes and motor response to supraorbital pressure.
- **Ophthalmoscopic Examination:** Use an ophthalmoscope to check for retinal column segmentation.
- **Pulse Examination:** Feel for carotid, radial, and femoral pulses bilaterally.
- **Auscultation:** Listen over the precordium for one minute and over the lungs for three minutes.
- **Clinical Observations:** Look for signs of rigor mortis or lividity.
- **Time of Death:** Record the time when all criteria are fulfilled.
- **Documentation:** Document all the above findings, date, and time of death in the patient's notes.
- **Hygiene:** Wash hands after completing the examination.

DEATH CERTIFICATION: The death certification is the official documentation, providing official confirmation of a person's death. Properly completing a death certificate is a significant responsibility for a physician/trained nurse.

DEATH CERTIFICATION FORM

This is to certify that:

Name of Deceased: [deceased's Name]	Sex: [deceased's Gender]	Age: [deceased's Age]
Date of Death: [write Date]	Date of Death: [write Date]	Place of Death: [write Place]

Cause of Death:

1. **Immediate Cause:** [Write Immediate Cause]
2. **Antecedent Cause:** [Specify Antecedent Cause]
3. **Underlying Cause:** [Indicate Underlying Cause]
4. **Other Significant Conditions Contributing to Death:** [Insert any other significant conditions]

CERTIFICATION

I hereby certify that I attended the deceased from [Write Date of First Attendance] to [write Date of Last Attendance] and that I last saw him/her alive on [Write Last Seen Date].

I further certify that death occurred on the date, time, and place stated above, to the best of my knowledge and belief, and that the cause(s) of death entered above are true and correct, to the best of my knowledge and belief.

Doctor Name: [Write your name]

Position: [Write your position]

Patient Registration Number: [Write medical record number]

Clinic/Hospital Address: [Write complete address]

Date: [Write date]

Signature: [Write signature]

NOTIFICATION OF DECEASED (TO: NEXT OF KIN / FAMILY REPRESENTATIVE)

Name of Relative and Relationship to Patient:	Relative's Signature:
Relative's ID Card Number:	Relative's Phone/cell number:

REQUESTING INVESTIGATIONS FOR HISTO-PATHOLOGY OF SPECIMEN AFTER PROCEDURE

On most forms you typically need to provide details about the

REQUESTING INVESTIGATIONS FORM (SAMPLE)

Date: 01-05-2024		Medical Record Number:	
Patient Name: Abbas Akhtar		Father/Husband Name: Noordad khan	
Age: 28 years old	Sex: Male	Marital status: Married	
Date of admission: 01-05-2024		Date of procedure: 02-05-2024	
Date of sending specimen: 02-05-2024		Time of procedure: 09:00 AM	
Short clinical history: A 28-year-old male with no known comorbidities (NKM) presented to the emergency room with the following complaints: 1. Right iliac fossa (RIF) pain – 2 days 2. Fever – 1 day 3. Vomiting – 1 day On examination, tenderness was noted upon palpation of the lower abdomen, particularly in the right iliac fossa. Additionally, during palpation of the left lower quadrant of the abdomen, pain was elicited, indicating a positive Rovsing's sign.			
Diagnosis:	Acute appendicitis		
Procedure Name:	Laparoscopic appendicectomy		
Consultant Name:	Dr. Junaid Ali (General Surgeon)		
Specimen Name:	Appendix		
Requesting for:	Histopathology		
Hospital Name:	J. hospital Pakistan		
Consulting Dept.	AKUH OR Dow lab OR SKMH		
Requesting Dept.	General surgery ward#02		
Special remarks:			
SINCERELY,			
[Your Name]	[Your Title/Position]	[Hospital/Department/Clinic Name]	

MEDICAL CERTIFICATE

TO WHOM IT MAY CONCERN

This is to certify that [Patient's Name], aged [Patient's Age], was under my care at [Hospital/Clinic Name] from [Start Date] to [End Date].

The patient was presented with symptoms consistent with dengue fever, including high fever, severe headache, joint and muscle pain, and a rash.

Upon further assessment and investigation tests, the patient was diagnosed with dengue fever.

Additionally, during the course of treatment, the patient was also found to be positive for malarial infection.

The patient received appropriate medical management, including antimalarial medications, intravenous fluids, and supportive care to manage both dengue fever and malaria.

Throughout the hospitalization period, the patient's condition was closely monitored, and necessary interventions were implemented to ensure optimal care.

SINCERELY,

[Your Name]	[Your Title/Position]	[Hospital/Department/Clinic Name]
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CONSULTATION REQUEST FORM

CONSULTATION REQUEST FORM

(Referral (a call) to specialist department for patient assessment)

Date:		Medical Record Number: [MRN]	
Name: [Patient's Full Name]		Ward number: Bed number:	
Age: [Patient's Age]	Gender: [Patient's gender]	Time of admission:	
Date of admission:		Requesting department:	
Referring Department: [Your Department]		Requesting Physician: [Physician Name]	
Referring Physician: [Your Name]		Date and Time:	
Date and Time:	Reason for Consultation: Patient has severe abdominal pain and absolute constipation from 3 days, we are suspecting intestinal obstruction		
Reason for Consultation: [Provide a brief summary of the patient's condition, including relevant medical history, presenting symptoms, and any pertinent findings from initial assessment or diagnostic tests.]			
Specific Questions/Concerns: [Detail any specific questions or concerns you have regarding the patient's condition or management that require input from the consulting department.]			
Current Medications: [List any medications the patient is currently taking, including dosage and frequency.]			
Diagnostic Tests/Results: [List any diagnostic tests that have been performed, along with relevant results and interpretations.]			
Clinical Findings: [Provide a summary of pertinent clinical findings from the physical examination or other assessments.]			
Treatment/Management Thus Far: [Describe any treatments or interventions that have been initiated for the patient's condition and their response to these interventions.]			
Requested Consultation: [Specify the department or specialty to which the consultation is being requested, along with any particular physician or team if applicable as mentioned above.]			
Additional Comments/Notes: [Include any additional comments or information that may be relevant to the consultation or patient management.]			
Referring Physician's Contact Information: [Provide your contact information, including phone number and email, for further communication or clarification if needed.]			
SINCERELY,			
[Your Name]	[Your Title/Position]	[Hospital/Department/Clinic Name]	

EXAMPLE OF SHORT URGENT CONSULTATION REQUEST

Reason for consultation: Urgent Consultation Request for Suspected Intestinal Obstruction
To: Surgery Department
Dear [Consulting Surgeon],

I am writing to request an urgent consultation for a patient under my care, [Patient's Name]. The patient presents with symptoms indicative of intestinal obstruction, including severe abdominal pain, constipation, and decreased gut sounds.

Given the seriousness of the situation and the need for prompt evaluation and management, I kindly request your expertise and assessment in this matter. Your timely intervention and recommendations would be greatly appreciated to ensure optimal patient care.

Thank you for your attention to this matter.

SINCERELY,

[Your Name]	[Your Title/Position]	[Hospital/Department/Clinic Name]
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DISCHARGE PLANNING & PATIENT SUMMARY

☞ **INTRODUCTION:** Refers to the process of preparing a patient for leaving the hospital or healthcare facility while providing a concise overview of their medical condition, treatment, and future care plans. This involves organizing necessary services, medications, and follow-up appointments, as well as creating a summary document detailing the patient's medical history, current status, and recommendations for ongoing care. The goal is to ensure a smooth transition for the patient from the healthcare setting back to their home or another care setting, with all essential information communicated effectively to the patient, their caregivers, and their primary care provider.

☞ **TYPES OF DISCHARGE:**

- 
1. **Planned Discharge:** Patient completes initial treatment and no longer requires direct hospital supervision.
 2. **DAMA:** Discharge against medical advice OR **LAMA:** Leave against medical advice.
 3. **Transfer:** Moving to another unit, ward, or hospital.
 4. **Abscond:** Leaving the hospital without prior notice.
 5. **Referral:** Being referred for further management.

☞ **IMPORTANT COMPONENTS FOR PLANNED DISCHARGE:**

1. Doctor's written order.
2. Discharge card.
3. Informing other departments.
4. Checking payment of bills.
5. Returning hospital belongings.
6. Arranging transport.
7. Documentation.

☞ **STEPS INVOLVED IN DISCHARGE PLANNING:**

1. Patient evaluation by qualified personnel.
2. Discussion with patients or relatives.
3. Planning for homecoming or transfer.
4. Assessing the need for caregiver training or support.
5. Referrals to home care agencies or support services.
6. Arranging follow-up appointments or tests.

☞ **SETTING THE SCENE (OPENING THE DISCUSSION):**

1. Introducing yourself to the patient and confirming their name and age for identification.
2. Summarize the situation.
3. Explore the impact of illness/hospitalization.
4. Assess current mood.
5. Discuss potential discharge.
6. Address concerns about going home.
7. Evaluate home situation and support.
8. Assess Activities of Daily Living (ADL).
9. Offer additional support services.
10. Discuss medication and compliance.
11. Address lifestyle changes.
12. Offer next follow-up appointment.
13. Advise on seeking medical help if needed.
14. Summarize and offer written information.
15. Confirm patient's understanding.
16. Address any further questions.
17. Express gratitude to say thanks to the patient.

HOSPITAL DISCHARGE SUMMARY FORM

REGISTRATION/MEDICAL RECORD NO: _____ BED _____ WARD _____

NAME: _____ SEX: _____ AGE: _____

DOA: _____ DOS/DOP: _____

INVESTIGATION:

SURGERY/PROCEDURE:

SURGEON NAME: _____ ASSISTANT: _____

OPERATIVE FINDINGS: _____

PRIMARY DIAGNOSIS: _____

SECONDARY DIAGNOSIS: _____

INPATIENT TREATMENT: _____

CONDITION AT THE TIME OF DISCHARGE: _____

DISCHARGE MEDICATION:

ADVICE TO THE PATIENT:

NEXT FOLLOW UP: _____ DRESSING: _____

Doctor Name	Doctor Title/Position	Hospital/Department/Clinic Name
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Doctor Title/Position

Hospital/Department/Clinic Name _____

TAKING CONSENT FOR DAMA/LAMA

PATIENT DISCHARGE AGAINST MEDICAL ADVICE (DAMA) CONSENT FORM

Patient Information

- Patient name:
- Date of birth:
- Address:
- Phone number:
- Patient medical record number:

Reason for Discharge Against Medical Advice: Please describe the reasons why you are choosing to leave the hospital against the medical advice provided by your healthcare team.

Understanding of Risks: I understand that leaving the hospital against medical advice may pose risks to my health, including exacerbation of my current condition, complications, and potential need for readmission.

Acknowledgment of Consequences: I acknowledge that by choosing to leave the hospital against medical advice, I may be assuming responsibility for any adverse outcomes that may occur as a result of my decision.

Discussion with Healthcare Provider: I have had a discussion with my healthcare provider (Doctor) regarding the risks and potential consequences of leaving the hospital against medical advice.

Patient's Signature: _____ **Date:** _____

Witness Signature (if applicable):

Witness Signature: _____ **Date:** _____

Healthcare Provider's (Doctor) Confirmation: I confirm that I have discussed the risks and consequences of discharge against medical advice with the patient and that they have made an informed decision.

Doctor Signature: _____ **Date:** _____

Patient Discharge Information and Consent Form

This is to certify that I, _____
a patient at _____ (fill in name of your hospital and ward), am
refusing at my own insistence and without the authority of and against the advice of my attending
physician(s) _____, request to leave against medical advice.

The medical risks/benefits have been explained to me by a member of the medical staff and I understand those risks.

I hereby release the medical center, its administration, personnel, and my attending and/or resident physician(s) from any responsibility for all consequences, which may result by my leaving under these circumstances.

PATIENT/NEXT OF KIN/RELATIVE'S CONFIRMATION

Patient name: _____

Patient ID Card Number: _____

Name of Relative and Relationship to Patient: _____

Relative's ID Card Number: _____

Time of leaving: _____

Patient signature: _____

Patient Phone/cell number: _____

Relative's Signature: _____

Relative's Phone/cell number: _____

Date leaving: _____

HEALTH CARE PROVIDER/HOSPITAL CONFIRMATION

Doctor Name: _____

Signature: _____

Date: _____

Doctor Title/Position: _____

Department/Ward/Bed No: _____

Hospital/Clinic Name: _____



FEVER OF UNKNOWN ORIGIN (FUO)

DEFINITION: Fever of unknown origin (FUO) is defined as a temperature of $> 100.9^{\circ}\text{F}$ ($> 38.3^{\circ}\text{C}$) lasting for > 3 weeks with no clear cause despite appropriate diagnostics. Infections, malignancy, and inflammatory or rheumatic conditions are the most frequent etiologies of fever of unknown origin (FUO).

DIFFERENTIAL DIAGNOSIS:

- » **Infectious:** Tuberculosis (TB), abdominal or pelvic abscess, UTI, catheter infections, pneumonia, typhoid fever, infective endocarditis, brucellosis, osteomyelitis, "Q" fever, viral infection (e.g., EBV, CMV, HIV)
- » **Gastroenterological:** Crohn's disease, ulcerative colitis, complicated cirrhosis, and alcoholic hepatitis
- » **Oncologic:** Lymphomas (HL, NHL), leukemias, melanoma, hepatic carcinoma, and renal cell carcinoma (RCC).
- » **Autoimmune:** Still's disease, SLE, polymyalgia rheumatica, cryoglobulinemia, polyarteritis nodosa (PAN), connective tissue disease, temporal arthritis, and granulomatous disease (including sarcoidosis).
- » **Endocrinologic:** Pheochromocytoma, hyperthyroidism, subacute thyroiditis.
- » **Miscellaneous:** Pulmonary emboli, stroke, post-MI syndrome, drug induced fever factitious fever (Munchausen syndrome), and familial mediterranean fever
- » **Undiagnosed (in 10–15% cases).**

DIAGNOSTIC WORKUP

For diagnosis start with a thorough history and physical exam, ask for family, social, sexual, occupational, dietary, and travel factors. Use minimal initial tests to guide further diagnostics. If the cause remains unclear, consider additional lab tests (like serology) and advanced imaging (like PET-CT or tissue biopsy).

Routine laboratory tests:

1. Obtain a CBC with differential.

Clues to infective causes where unclear

- » **↑ Lymphocytes (Lymphocytosis):** viral infection, rubella, infectious mononucleosis, mumps), pertussis, brucellosis, and Chronic infections (Tuberculosis, syphilis, toxoplasmosis), HL, NHL and CLL.
- » **↓ Lymphocytes (Lymphocytopenia):** Infections (sepsis, measles, miliary TB, HIV), Legionella, steroids.
- » **↑ White blood cells (Leukocytosis):** Infections, Sepsis, Leukemia → leads to increased release of premature leukocytes into the blood (AML, ALL, CLL, CML) and drugs (lithium)
- » **↓ White blood cells (Leukopenia):** Typhoid fever, typhus, chikungunya infection, zika fever, acute HIV infection, aplastic anemia, SLE, rheumatoid arthritis and **Viral hemorrhagic fevers** such as dengue fever, lassa fever, ebola fever, crimean-congo hemorrhagic fever, hanta fever, yellow fever.
- » **↑ Neutrophils (Neutrophilia):** Bacterial infection (especially pyogenic, due to *S. aureus*, *S. pneumoniae*)
- » **↓ Neutrophils (Neutropenia):** Sepsis, viral, brucella, typhoid, kala-azar, TB, aplastic anemia, Hepatitis
- » **↑ Eosinophils (Eosinophilia):** Parasites (Strongyloidiasis, Schistosomiasis, Trichinellosis), Drugs (macrolides, allopurinol), Polyarteritis nodosa, Aspergillus infection, CML and Hodgkins disease
- » **↓ Eosinophils (Eosinopenia):** Infections (typhoid fever, paratyphoid fever, sepsis)
- » **↓ Platelets (Thrombocytopenia):** Malaria (parasites on film indicative), CML, EBV

2. LFTs: Hepatitis, cholangitis, alcoholic liver disease.

3. Inflammatory markers for Acute phase: ESR and CRP.

4. Urinalysis and urine culture: if the patient history is suggestive of UTI.

5. Blood culture: THREE SETS of culture should always be obtained, preferably when the patient has not taken antibiotics for several days and should be held by the laboratory for 2 weeks to detect slow-growing organisms.

Specific tests based on history/Exam findings:

1. Thyroid function test: Serum TSH or/Free T4 and thyroid antibodies test for thyroid dysfunction
 2. Lumbar puncture: If there is any suggestion of CNS infection – headache, neck stiffness, delirium.
 3. Sputum gram stain and sputum culture
 4. Serum protein electrophoresis (SPEP)
 5. If ones suspected of Tuberculosis: culture of urine, sputum, stool, CSF and morning gastric aspirates.
- Other tests: ANA, Rh factor, CK, dsDNA, ANCA, anti-CCP, PCR, viral cultures, and viral serologies/antigen tests).
- Imaging: Obtain a CXR, CT chest, abdomen, and pelvis should be done early in the workup of a true FUO.
- Invasive testing (marrow/liver biopsy) generally low yield. Laparoscopy and colonoscopy are higher yield as second-line tests (after CT).



EXAMPLES OF PHYSICAL FINDINGS WITH PARTICULAR SIGNIFICANCE IN PATIENTS WITH FEVER OF UNKNOWN ORIGIN

Location/sites	Physical finding	Possible differential diagnosis
Head	Sinus tenderness	Sinusitis
Temporal artery	Nodules, cord or reduced pulsations	Temporal arthritis
Oropharynx	Ulceration, tender tooth	Dental abscess, Aphthous stomatitis, Herpangina, SLE, Behcet disease, Disseminated histoplasmosis or blastomycosis, Crohn's disease
Fundi or conjunctivae	Choroid tubercle, petechiae	Disseminated granulomatosis, endocarditis
Thyroid	Enlargement, nodules, tenderness	Thyroiditis (e.g., subacute thyroiditis, Hashimoto's thyroiditis), thyroid nodules, Graves disease
Heart	Murmurs, rubs, gallops	Infective endocarditis, myocarditis, pericarditis, valvular heart disease
Abdomen	Hepatomegaly, splenomegaly, masses, tenderness, enlarge iliac crest lymph nodes	Hepatitis, liver abscess, splenic abscess, intra-abdominal malignancy, lymphoma, inflammatory bowel disease, Disseminated granulomatosis
Rectum	Masses, tenderness, blood in stool	Hemorrhoids, anal fissures, colorectal cancer, proctitis
Genitalia	Ulcers, lesions, discharge, inflammation	Sexually transmitted infections (e.g., herpes simplex virus, syphilis, gonorrhea), genital ulcers syndrome (e.g., Behcet's disease), genital warts, vulvovaginal candidiasis
Lower extremities	Leg swelling, erythema, warmth	Deep vein thrombosis, thrombophlebitis, cellulitis, peripheral artery disease
Skin and nails	Rash, petechiae, purpura, splinter hemorrhage, subcutaneous nodules, clubbing	Infectious diseases (e.g., cellulitis, abscesses), autoimmune disorders (e.g., SLE), vasculitis, drug reactions and endocarditis
Lymph nodes	Generalized adenopathy Regional/localized adenopathy	HIV, Primary EBV, histoplasmosis Lymphoma, cat scratch disease, toxoplasmosis

FEVER WITH CHILLS & RIGORS

Fever with chills without localizing symptoms.

Differential diagnosis

- » Malaria
- » Viral: Dengue, COVID-19
- » Urinary tract infections (UTI)
- » Pyelonephritis
- » Septicemia
- » Collection of pus in body
- » Infective Endocarditis
- » Kala azar
- » Cholangitis

Diagnostic workup

- » CBC
- » Malaria Parasite
- » Dengue NS1 (+ve within <7 days of symptoms)
- » Dengue IgG & IgM
- » Urinalysis, Urine culture for UTI.

Rx

(Tab. Artem DS plus, Tab. Artheget DS plus)

1. **Tab. Artemether + Lumefantrine** (Artem DS, Artheget DS)
 - » Tab. Artem DS → 1-1-1 (TDS) for 3 days
 - » Tab. Artem DS Plus → 1-0-1 (BD) for 3 days
2. **Cap. Cefixime 400mg** (Cefim, Cefspan, Cefiget)
OR **Cap. Azithromycin 500mg** (Azomax, Zetro)
0-0-1 (OD)
OR **Tab. Ciprofloxacin 500mg** (Ciplet, Novidate)
OR **Tab. Levofloxacin 250mg**
1-0-1
3. **Tab. Paracetamol** (Panadol, Calpol, Febrol)
1-1-1 (1-2 tablets = 500-1000mg x TDS)
4. **Syp. Multivitamins/appetizer** (Lysovit, Glyvesol)
2 Teaspoonful x BD

SEPSIS

Name:
Temperature:Age:
B.P.:Sex:
Pulse:Date:
Resp. Rate:

DEFINITIONS AND CRITERIA IN THIS SECTION APPLY TO ADULT PATIENTS.

THIRD INTERNATIONAL CONSENSUS DEFINITIONS FOR SEPSIS AND SEPTIC SHOCK

- Severe sepsis: a severe, life-threatening condition that results from a dysregulation of the patient's response to an infection, causing tissue and organ damage and subsequent organ dysfunction.
- Septic shock: a sepsis syndrome accompanied by circulatory and metabolic abnormalities that can significantly increase mortality.

Diagnostic criteria

- Persistent hypotension: Vasopressors are required to maintain MAP ≥ 65 mm Hg.
- Persistent lactic acidosis: Lactate > 2 mmol/L (18 mg/dL) despite adequate fluid resuscitation.

Other definitions of sepsis syndromes.

- Systemic inflammatory response syndrome (SIRS) criteria: a combination of physiological and immune responses by the to an infection or noninfectious insult such as acute inflammatory process or trauma.
 - At least 2 of the following 4 criteria are required to define SIRS:
 - Temperature: $> 100.4^{\circ}\text{F}$ or $< 96.8^{\circ}\text{F}$ ($> 38^{\circ}\text{C}$ or $< 36^{\circ}\text{C}$)
 - Heart rate: $> 90/\text{minute}$
 - Respiratory rate: > 20 per minute or $\text{PaCO}_2 < 32$ mm Hg
 - White blood cell (WBC) count: $> 12,000/\text{mm}^3$ or $< 4,000/\text{mm}^3$ or $> 10\%$ immature bands
- Sepsis: SIRS criteria PLUS a suspected or confirmed underlying infection
- Severe sepsis: sepsis PLUS dysfunction of at least one organ or system
- Multiple organ dysfunction syndrome (MODS)
 - Progressive & potentially reversible failure in the physiologic function of several organs &/or systems
 - The more organs that are affected, the greater the mortality risk.
- Bacteremia: the presence of bacteria in the bloodstream, confirmed on blood cultures.

SOFA Score (Sequential organ failure assessment score)

- Used in critical care settings as a tool to identify organ failure and predict mortality.
- The score should be calculated after 24 hours of ICU admission and then every 48 hours.
- Should not be used to diagnose sepsis

System	0 points	1 points	2 points	3 points	4 points
Respiration: PaO ₂ /FIO ₂ (mmHg)	≥ 400	< 400	< 300	< 200 with respiratory support	< 100 with respiratory support
Coagulation: Platelets $\times 10^3/\text{mm}^3$	≥ 150	< 150	< 100	< 50	< 20
Liver: Bilirubin (mg/dL)	< 1.2	1.2–1.9	2.0–5.9	6.0–11.9	> 12.0
Cardiovascular system	MAP ≥ 70 mmHg	MAP < 70 mmHg	Dopamine < 5 mcg/kg per min for ≥ 1 hour OR dobutamine at any dose	Dopamine $> 5.1 - 15$ mcg/kg per min for ≥ 1 hour OR epinephrine ≤ 0.1 mcg/kg/min for ≥ 1 hour OR norepinephrine ≤ 0.1 mcg/kg/min for ≥ 1 hour	Dopamine > 15 mcg/kg per min for ≥ 1 hour OR epinephrine > 0.1 mcg/kg/min for ≥ 1 hour OR norepinephrine > 0.1 mcg/kg/min for ≥ 1 hour
Central nervous system: Glasgow Coma Scale	15	13–14	10–12	6–9	< 6
Renal function: Creatinine (mg/dL)	< 1.2	1.2–1.9	2.0–3.4	3.5–4.9 OR urine output < 500 mL/day	> 5.0 OR urine output < 200 mL/day

Interpretation

- SOFA score (≥ 2 points): overall mortality risk = 10%



CLINICAL FEATURES

- » Fever, chills, and diaphoresis
- » Tachycardia
- » Tachypnea (see SOFA score)
- » **Features of organ dysfunction**
 - **CNS impairment:** altered mental status.
 - **Cardiovascular failure:** hypotension
 - **Coagulopathy** → Disseminated Intravascular Coagulation (DIC) → petechiae, purpura
 - **Liver failure:** jaundice
 - **Kidney failure:** oliguria
 - **Respiratory failure:** symptoms of acute respiratory distress syndrome (ARDS)
- » **Additionally in septic shock**
 - Hypotension (MAP < 65 mmHg)
 - Initially warm skin and normal capillary refill time (warm shock) → cold cyanotic, pale, or mottled skin with prolonged capillary refill time (cold shock)
- » Features of the primary infection
- » Generalized edema (capillary leak).

DIAGNOSTIC WORKUP

Apart from serum lactate and blood cultures (minimum two sets), the following laboratory tests should be conducted to confirm the diagnosis and assess for organ dysfunction.

- » **CBC:** findings are variable.
 - Leukocytosis or leukopenia
 - Thrombocytosis or thrombocytopenia
- » **CRP, procalcitonin:** typically, elevated.
- » **BUN & creatinine:** ↑ BUN and ↑ creatinine
- » **Glucose:** hyperglycemia, hypoglycemia
- » **Serum electrolytes:** Electrolyte imbalance
- » **LFTs:** ↑ bilirubin, ↑ INR, ↑ ALT, ↑ AST
- » **Coagulation panel:** ↑ prothrombin time, ↑ activated partial thromboplastin time, ↓ antithrombin-III.
- » **D-dimer:** ↑ D-dimer may be present.
- » **Serum amylase and lipase:** consider if pancreatitis is suspected.
- » **ABGs:** to identify possible acid-base disturbances and assess oxygenation.

Identifying the source of infection

- » In addition to blood cultures, consider extra cultures guided by clinical decisions.
 - Urine culture
 - Sputum culture
 - Consider also culture of: CSF, wound secretion, tissue/fluid.
- » **Diagnostic procedures** as indicated to obtain samples for cultures (e.g., lumbar puncture, thoracentesis, paracentesis, arthrocentesis)

Rx

TREATMENT OF SEPSIS

- » Stabilize patient using ABCD&E
- » Establish large-bore intravenous (IV) access.
- » **Vitals monitoring:** Check BP, PR, RR, Temperature, SpO₂
- » Provide supplemental oxygen.
- » Monitor and record input/output.
- » **Obtained initial laboratory tests:** serum lactate and Two sets of blood cultures. **Additional Labs:** CBC, LFTs, BUN, S/Electrolytes, Procalcitonin, CRP, S/calcium, PT/INR, ABGs and D-Dimer.
- » **Identify patients with septic shock:** Hypotension, elevated lactate.
- » **IV fluid:** Initial fluid resuscitation with 30 mL/kg of crystalloid.
- » **Correct electrolyte imbalance**
- » **Vasopressors if shock persists despite adequate fluid therapy:**
 - » **Inj. Norepinephrine 4mg (Levophed) – first line drug**
 - **Dose range:** 2.5–0.3 mcg/kg/minute.
 - **Compatible solution:** Dextrose 5% water (D5W)
 - **Single Dilution:** 4mg/4ml in 46ml D5W = 80mcg/ml
 - **Double dilution:** 8mg/8ml in 42ml D5W = 160mcg/ml
 - » Consider as alternate vasopressors in select cases, or as an additional vasopressor for refractory tissue hypoperfusion.
 - » **Inj. Dopamine 200mg/5ml**
 - **Dose range:** 2.5–20 mcg/kg/minute.
 - **Compatible solution:** D5W or 0.9% NS
 - **Single Dilution:** 200mg/5ml in 45ml D5W or 0.9% NS, Final strength = 4000mcg/ml or 4mg/ml.
 - **Double dilution:** 400mg (2-Ampule) in 40ml D5W/NS, Final strength = 8000mcg/ml or 8mg/ml.
 - » **Inj. Dobutamine 250mg/20ml**
 - **Dose range:** 2.5–20 mcg/kg/minute.
 - **Compatible solution:** D5W or 0.9% NS
 - **Dilution:** 250mg/20ml in 30ml D5W or 0.9% NS, Final strength = 5000mcg/ml or 5mg/ml.
- » **Start empiric antibiotic regimens for sepsis with unclear source (Ideally within the first hour after the obtain blood culture).**
 - » **Inj. Vancomycin 500mg to 1g (Vancotic, Vinjec) x IV x TDS,** diluted in 100ml 0.9% Normal saline and administer slowly over at least 60 min at a rate of 10mg/min to prevent adverse infusion reactions. **Dosage: 15mg/kg IV every 8-12 hour.**
 - » **PLUS, one of the following:** The preferred approach is to dilute all injections with 100ml of 0.9% Normal Saline (NS).
 - » **Inj. Piperacillin/Tazobactam 4.5g (Tazbac, Tanzo) x IV x TDS**
 - » OR **Inj. Meropenem 1g (Meronem, Penro) x IV x TDS**
 - » OR **Inj. Ceftriaxone 2g (Oxidil, Rocephin) x IV x OD**
 - » OR **Inj. Cefepime 2g (Cefstar, Uceph) x IV x TDS**
 - » **For fever:** **Inj. Paracetamol 1g/100ml (Provas) x IV x TDS**
 - » **Inj. Esomeprazole 40mg (Nexum, Esso) x IV x OD** diluted with 100ml of 0.9% Normal Saline (NS).
 - » **Thromboembolism (VTE) prophylaxis:**
 - » **Inj. Enoxaparin sodium 80mg (Clexane) x 100 IU/kg (1.5mg/kg) x subcutaneously (SC) x OD**
 - » **Alternative:** **Inj. Fondaparinux (Arixtra) 5-10mg x SC x OD**

TYPHOID FEVER (ENTERIC FEVER)

- Pathogen: *Salmonella typhi* (enterica serotype typhi - Gram-negative rod)
- Transmission: fecal-oral → **Direct**: person-to-person contact from contaminated stool via handshake to the next person and **Indirect**: contaminated food and water.
- Incubation period: 5–30 days (most commonly 7–14 days)
- If left untreated, three different disease stages, each lasting a week, classically occur.
- After 3 weeks of disease: slow regression of symptoms; patients may become chronic salmonella carriers

Stages of Clinical features

WEEK-1

- Fever – Stepladder pattern (Low fever then gradually increases)
- Relative bradycardia, Headache

WEEK-3

- Presence of clinical features of week-2
- Additional possible complications**
 - Gastrointestinal ulceration with bleeding and perforation
 - Hepatosplenomegaly
 - In rare cases: sepsis, meningitis, myocarditis, and renal failure

DIAGNOSTIC WORKUP

- Most accurate test:** Blood culture is the most important diagnostic test at disease onset, as stool cultures are often **-ve** despite active infection. Blood culture, which is **+ve** in the 1st week of illness in 80% of patients who have not taken antibiotics therapy.
- CBC:** Anemia (↓Hb), Thrombocytopenia Leukopenia or leukocytosis
- LFTs:** maybe abnormal (Transaminitis)
- USG abdomen:** Hepatosplenomegaly.
- Gold standard:** Bone marrow culture occasionally **+ve** but rarely performed

TREATMENT GUIDELINE

Complicated or severe infections (see emergency/ER section) – UPTODATE Guidelines

- IV Ceftriaxone 2g (Oxidil) x OD/BD
- OR IV Levofloxacin 750mg (Leflox) x OD
- OR IV Meropenem 1-2g x TDS
- Duration: 7–14 days

Treatment for carrier: (CMDT2024)

- Tab. Ciprofloxacin 500-750mg (Hiflox, Quinolox) x BD for 4 weeks.

Definitive treatment: *Salmonella* bacterial may sequester in the gallbladder.

Cholecystectomy may be required if prolonged antibiotics therapy fails.

Prevention: *Salmonella* infection is best prevented by protecting the water supply, preventing fecal contamination during food production, cooking and refrigerating foods, pasteurizing milk and milk products, and handwashing before preparing foods.

WEEK-2

- Persistent fever, but no chills; mostly unresponsive to antipyretics
- Rose-colored skin spots:** a small, speckled, rose-colored exanthem that appears on the lower chest and abdomen (most commonly around the navel) in approximately 30% of cases.
- Tongue:** Greyish/yellowish-coated tongue with red edges
- Non-specific abdominal pain and headache**
- Yellow-green diarrhea;** comparable to pea soup (caused by purulent, bloody necrosis of the Peyer patches) or obstipation & bowel obstruction (due to swollen Peyer patches in the ileum)
- CNS features:** Altered sensorium, delirium, seizures, and coma



TREATMENT OF TYPHOID FEVER (ENTERIC FEVER)

- Tab. Ciprofloxacin 750mg** (Hiflox, Ciproxen) twice daily for 5 days
OR **Tab. Levofloxacin 500mg** (Leflox) x Once daily (OD)
Duration: 5-7 days for uncomplicated and 10-14 days for severe enteric infection. (Ref: CMDT 2024)
OR **Tab. Azithromycin 500mg** (Azomax, Azitma) x 1g (2 tablets) once daily (OD) then 500mg OD for 5-7 days
OR **Cap. Cefixime 400mg** (Cefspan, Cefiget, Cefim) 1-0-1 (BD) x for 5-7 days [at dose: 20mg/kg/day]
- Tab. Paracetamol 500mg** (Calpol, Febrol, Panadol) 1-1-1 (TDS) or 2-2-2 (TDS) [at dose 500mg – 1000mg (1-2 tablets) x 3-4 times per day. **Maximum:** 4g/day]
OR **Tab. Mefenamic acid 500mg** (Ponstan fort, Mefnac DS) x TDS
- Syp. Multivitamins/appetizer** (Lysovit, Leaderplex, Glyvesol) 2-0-2 (2 teaspoonful twice daily)

With epigastric upset/peptic ulceration:

- Cap. Omeprazole 40mg** (Ruling, Risek)
OR **Cap. Esomeprazole 40mg** (Esso, Nexum) 1-0-0 (OD)
کھانے سے 30 منٹ پہلے

With nausea or/ vomiting:

- Tab. Domperidone 10mg** (Motilium, Domel) x TDS
OR **Syp. Domperidone 1mg/1ml** (Motilium, Domel) x 2TSF x TDS
کھانے سے 30 منٹ پہلے



MALARIA FEVER

- Organism: Plasmodia – Eukaryotic parasites (belonging to the Sporozoa group)
- Vector: the female Anopheles mosquito. Host: humans
- Partial resistance against malaria
 - Carriers of sickle-cell mutation
 - Individuals with either certain Duffy antigens or no Duffy antigens are resistant to *P. vivax* & *knowlesi*
 - Other hemoglobinopathies (e.g., thalassemia, HbC)

Classic disease and fever patterns of different plasmodium species

Species of plasmodium	Disease	Fever spikes
<i>Plasmodium vivax</i> & <i>P. ovale</i>	Tertian malaria (usually less severe)	Every 48 hours
<i>Plasmodium malariae</i>	Quartan malaria (usually less severe)	Every 72 hours
<i>Plasmodium falciparum</i>	malignant tertian malaria (most severe form)	Irregular
<i>Plasmodium knowlesi</i>	Quotidian malaria	Every 24 hours

Clinical features

Course: Infection → asymptomatic parasitemia → uncomplicated illness → severe malaria → death

General symptoms

- An acute attack of malaria typically begins with a prodrome of headache and fatigue, followed by fever.
- A classic malarial paroxysm includes chills, high fever, and then sweats (Diaphoresis)
- Patients may appear to be remarkably well between febrile episodes.
- High fever: Fever spikes occurring at regular intervals are no longer commonly observed.
 - Quotidian malaria: fever spikes every 24 hours.
 - Tertian malaria: periodic fever spikes every 48 hours.
 - Quartan malaria: periodic fever spikes every 72 hours.
 - Malignant tertian malaria (associated with *falciparum* malaria):
 - Irregular fever spikes without a noticeable rhythm

The risk for *falciparum* malaria is greatest within 2 months of return from travel an endemic area; other species may cause disease many months—and occasionally more than a year—after return from an endemic area

Organ-specific symptoms

- Blood: Thrombocytopenia (↑ bleeding risk), Hemolytic anemia (weakness, paleness, dizziness)
- Gastrointestinal: Nausea, vomiting, diarrhea, abdominal pain and anorexia (Loss of appetite)
- Musculoskeletal: myalgias, arthralgia, back pain sometime
- Liver: mild hepatomegaly, splenomegaly, discrete jaundice
- CNS: hallucinations, confusion, impaired consciousness, seizures (may represent simple or febrile), coma

Classification

- Uncomplicated malaria: can be caused by all six *Plasmodium* species, symptomatic, diagnostically proven malaria without features of severe malaria.
- Severe malaria

- Description: potentially fatal manifestation or complication of malaria
- Etiology: most commonly a result of *falciparum* malaria
- Pathophysiology: Infected erythrocytes occlude capillaries, which can lead to severe organ dysfunction.
- Criteria for severe malaria: ≥ 1 of the following in a patient with proven malaria
- Clinical findings
 - General: Prostration (an extreme physical weakness or exhaustion → unable to move or function normally.
 - CNS: Hallucinations, confusion, impaired consciousness, seizures, coma
 - Cardiac: Shock (hypotension, capillary refill time ≥ 3 seconds), heart failure
 - Pulmonary: Respiratory distress, pulmonary edema, ARDS
 - Renal: Flank pain, oliguria, hemoglobinuria, acute kidney injury
 - Gastrointestinal: Jaundice
 - Hematopoietic: Significant bleeding
- Laboratory findings
 - Severe anemia: Hb < 7 g/dL in adults, < 5 g/dL in children
 - Hypoglycemia: Blood sugar level < 40 mg/dL
 - Acidosis (with or without lactemia): Base deficit > 8 meq/L or bicarbonate < 15 meq/L
 - Hyperlactatemia: Serum lactate > 5 meq/L
 - Acute kidney injury (AKI): Creatinine > 3 mg/dL or urea > 20 mmol/L
 - Hyperbilirubinemia: Serum bilirubin > 3 mg/dL
 - High malaria parasitemia: Blood parasitemia greater than 5% or greater than 200,000 parasites/μL.

Rash and lymphadenopathy are not typical in malaria, and thus suggestive of another cause of fever

△ Malaria fever C/C:

Diagnosis is based on clinical presentation and laboratory investigations

Laboratory investigation:

Complete blood count (CBC)

- » Anemia: ↓ Hb
- » Possibly leukopenia: WBCs < 4,500/ μ L
- » Thrombocytopenia: Platelets < 150,000/ mm^3
- » Hemolytic anemia: ↓ Hemoglobin, ↓ Haptoglobin, ↑ Serum LDH, ↑ Reticulocytes, ↑ indirect bilirubin
- » Blood sugar: Hypoglycemia
- » Urea and creatinine: AKI
- » Serum creatinine: may be abnormal
- » ABGs

Urine D/R: Hemoglobinuria may occur with intravascular hemolysis.

Giemsa-stained blood smears remain the mainstay of diagnosis.

- » Best initial test: thick blood smear
- » High sensitivity
- » Detects the presence of parasite.

- » Confirmatory test: thin blood smear
- » Lower sensitivity than thick blood smear, but higher specificity

Findings include:

- Schuffner granules (fine, brick-red dots) within RBCs infected with *P. vivax* and *ovale*.
- Crescent-shaped gametocytes

Rapid antigen detection test: MP ICT test (more rapid but less sensitive)

Additional considerations in *P. vivax* and *P. ovale* → Check G6PD activity levels.

Treat malaria as falciparum until proven otherwise



Non-Falciparum Malaria

P. vivax, *P. ovale* (tertian malaria) without chloroquine resistance

1. Tab. Chloroquine 250mg (Resochin, Nivaquine-P)

Dosage: 1g (4 tablets) loading dose followed by 500mg (2 tablets at 6h, 24h & 48h OR at dose 25 mg/kg body weight divided over 3 days, i.e. 10 mg/kg on day 1, 10 mg/kg on day 2 and 5 mg/kg on day 3.

OR Tab. Hydroxychloroquine 200mg (HCQ, Plaquenil, Plaquin H) at initial dose of 800 mg (4 tablets) followed by 400 mg (2 tablets) in 6-8 hours and 400 mg (2 tablets) on each of 2 consecutive days

- » Plus one of the following: Tab. Primaquine 7.5 mg (4 tab = 30mg) x OD/BD for 14 days or Tab. Tafenoquine 150mg (2 tablets) x Once

P. vivax, *P. ovale* (tertian malaria) with chloroquine resistance

» Tab. Artemether + Lumefantrine (Artem, Gen-M, Arceva)

↳ Strength available: 20/120mg, 40/240mg, 80/480mg

↳ Tab. Gen-M or Tab. Artem 40/240mg x TDS for 3 days

↳ Tab. Gen-M or Tab. Artem 80/480mg x BD for 3 days

» OR Tab. Atovaquone + Proguanil

» OR Tab. Quinine 650mg x TDS PLUS Cap. Doxycycline 100mg (Doxyn, Vibramycin) OR Cap. Clindamycin 300mg (Dalacin-C) x BD for 7 days.

- » Plus one of the following: Tab. Primaquine 7.5 mg (4 tab = 30mg) x OD/BD for 14 days OR Tab. Tafenoquine 150mg (2 tablets) x Once

2. Tab. Paracetamol 500mg (Panadol, Calpol, Febrol) 1-1-1 (TDS) or 2-2-2 (TDS)

3. Syp. Multivitamins/appetizer (Lysovit, Leaderplex, Tresorix forte) 2-0-2 (2 teaspoonful two times a day)



Un-complicated Falciparum Malaria

1. Tab. Artemether + Lumefantrine (Artem, Gen-M, Arceva)

↳ Strength available: 20/120mg, 40/240mg, 80/480mg

↳ Tab. Gen-M or Tab. Artem 40/240mg x TDS for 3 days

↳ Tab. Gen-M or Tab. Artem 80/480mg x BD for 3 days

» OR Tab. Artesunate (AS) + Sulfadoxine/Pyrimethamine (SP)

Drug brand: Genart-SP, Sinda-MP

Blister pack with 6 tablet AS 100mg and 3 tablet SP 500/25mg

Dose: Day-1: 2 tab AS + 3 tab SP. Day-2: 2 tab AS. Day-3: 2 tab AS

(Dipip 40/320mg or Diphos or Neo-Fansidar)

- » OR Tab. Dihydroartemisinin 40mg + Piperaquine 320mg
2-0-2 (4 tab/day for 3 days)

2. Tab. Paracetamol (Panadol, Calpol) 1-1-1 (TDS), 2-2-2 (SOS)

3. Syp. multivitamins/appetizer 2-0-2 (2 TSP Two times a day)

کھاتے سے 30 منٹ پہلے

Plasmodium falciparum is resistant to chloroquine and Sulfadoxine-pyrimethamine in most areas, and falciparum malaria should not be treated with these older drugs.

FOR NAUSEA &/OR VOMITING

4. Tab. Domperidone 10mg (Motilium, Domel) x TDS

OR Syp. Domperidone 1mg/1ml (Motilium, Domel) x 2TSF x TDS

کھاتے سے 30 منٹ پہلے

Severe malaria is a medical emergency - see treatment detail in Emergency medicine portion



DENGUE FEVER

- ☛ **Introduction:** Dengue fever is a viral infectious disease caused by a flavivirus (DENV-Serotype 1-4) transmitted primarily from human to human through the bites of infected mosquitoes, *Aedes aegypti* and *Aedes albopictus*, which breeds in standing water; collections of water in containers, water-based air coolers and tyre dumps are a good environment for the vector in large cities. It is endemic in Asia ((Thailand, Pakistan, India, Bangladesh), the Pacific, Africa and the Americas
- ☛ **The course follows 3 phases:** febrile, critical, and convalescent (recovery) phase. In dengue haemorrhagic fever or dengue shock syndrome all **3 STAGES** can be observed. In dengue fever, critical phase is normally bypassed.
- ☛ **Incubation period:** 3-10 days after mosquito bite, dengue begins abruptly after a typical incubation period.

CLINICAL FEATURES OF DENGUE FEVER

☛ Dengue without warning signs (Febrile phase)

- » **Duration of febrile phase of dengue fever:** usually lasts 2-7 days
- » **Clinical features:**
 - ☛ Sudden onset of **High fever** (up to 104.0°F or 40°C) **PLUS TWO** of the following symptoms during the febrile phase indicate dengue fever (but not meeting the case definition of dengue haemorrhagic fever)
 1. Severe headache
 2. **Retro-orbital eye pain**
 3. Severe arthralgia and myalgia (often referred to as "**break-bone fever**")
 4. Maculopapular, measles-like exanthem (typically appears 2-5 days after fever onset)
 5. Generalized lymphadenopathy.
 - ☛ **Positive capillary fragility test or a positive tourniquet test** (inflate BP cuff to midway between systolic and diastolic for 5 minutes ≥ 10 petechiae/inch²)
 - ☛ **Children are usually asymptomatic**

☛ Dengue with warning signs (Critical phase)

- » **Critical phase:** increased risk of clinical deterioration that occurs 3-7 days after symptom onset (coincides with fever abatement/subsiding)
- » **At risk population associated with severe disease:** Individuals with a history of previous dengue infection, Infants, extreme age, obesity, pregnancy, patients with severe comorbidities (e.g., diabetes mellitus, Hypertension, renal impairment, hemolytic diseases)
- » **Clinical features:**
 1. Abdominal pain
 2. Persistent vomiting
 3. Lethargy or restlessness
 4. **Hepatomegaly:** Liver enlargement > 2 cm
 5. **Signs of clinical fluid accumulation/plasma leakage:** e.g., pleural effusion and/or ascites
 6. **Hemorrhagic manifestations:** e.g., petechiae, epistaxis, gingival/mucosal bleeding
 7. **CBC tests:** increase in hematocrit (Hct) concurrent with rapid decrease in platelet count.

☛ Clinical features of Dengue hemorrhagic fever (DHF)

- » DHF typically occurs as a result of an antibody-dependent reaction in patients who are reinfected with a different serotype. Generally, develops as the initial fever subsides (defervescence) between day 3 - 8 of the illness. The period of clinically significant plasma leakage usually lasts between 24 - 48 hours.

» Clinical features:

1. Temperature changes ranges from hypothermia to a second spike in fever
2. **Evidence of severe hemorrhagic manifestations** (e.g., petechiae, ecchymoses, purpura, hematemesis, melena) or a positive tourniquet test due to **thrombocytopenia** (platelets $< 100,000/\text{mm}^3$)
3. **Severe organ involvement:** Hepatomegaly, liver failure, impaired consciousness, confusion, $\downarrow$ GCS
4. **Sign of clinical fluid accumulation:** Pleural effusion, ascites, abdominal pain, respiratory distress

☛ Clinical features of Dengue shock syndrome (DSS)

- » **DSS has all the criteria of DHF plus circulatory failure as evidenced by:**
 - Rapid and weak pulse and narrow pulse pressure, or
 - Age-specific hypotension and cold, clammy skin and restlessness.

Convalescent (Recovery) phase

- ▀ Patients who survive the 24–48-hour critical period will begin to reabsorb the extravasated fluids that leaked from the intravascular space (e.g., plasma and administered intravenous fluids)
- ▀ The following may be observed during this period:
 1. Patient will report a sense of improved wellbeing, return of appetite, increased urine output
 2. Hemodynamic status stabilizes/vital signs stabilizing (widen pulse pressure, strong palpable pulse)
 3. Hematocrit levels returning to normal or low due to dilutional effects of the reabsorbed fluid
 4. WBC count start to rise soon after defervescence (fever subsides)
 5. Increase in platelet count but it takes a longer time than WBCs to become normal

DIAGNOSTIC WORKUP

- ▀ Diagnosis is based on clinical presentation and laboratory investigations.
- ▀ Complete blood count (CBC)
 - ▀ Leukopenia: WBCs $< 4,500/\mu\text{L}$
 - ▀ Neutropenia: Neutrophil count (mild: 1000–1500 cells/ μL ; moderate: 500–1000 cells/ μL ; severe: < 500 cells/ μL)
 - ▀ Thrombocytopenia: Platelets $< 150,000/\text{mm}^3$
 - ▀ Haematocrit (Hct): Elevated due to dehydration (or reduced in DHF due to plasma leakage)
- ▀ Confirmatory tests
 - ▀ Acute phase (≤ 7 days after symptom onset)
 1. Dengue NS1 test (Dengue non-structural protein-1 antigen test): Positive
 2. Dengue RNA PCR: Test of choice for viral nucleic acid detection and can be ordered within the first 5 days.
 3. Immunohistochemistry tests (IHC) tests for antigen detection in tissue samples and dried blood spots.
 - ▀ Convalescent (Recovery) phase (> 7 days after symptom onset)
 1. Serologic tests: Dengue IgM & IgG (may be negative in the first 5 days of illness)
 2. Dengue RT-PCR RNA
 3. Tissue test: Immunohistochemistry tests (IHC) tests
- ▀ LFTs: Elevated AST or ALT ≥ 1000 U/L
- ▀ Chest x-ray: Only required if DHF/DSS is suspected, may show blunting of the costophrenic angles in erect position due to pleural effusion in the early phase of plasma leakage (severe disease).
- ▀ Ultrasound abdomen: Only required if DHF/DSS is suspected, may show ascites, abnormalities of liver/gallbladder (severe disease)

STEPWISE TREATMENT APPROACH OF DENGUE FEVER

- ▀ The most commonly used and practical treatment plan is produced by WHO based on the severity of infection.
- ▀ The WHO classification separates patients into 1 of 3 groups: Group-A (Treated at home), Group-B (require hospital admission) or Group-C (require emergency treatment), depending on the clinical presentation.

**WHO GROUP-A (Dengue with no warning signs)
HOME/OUTPATIENT MANAGEMENT**

- ▀ **Group-A patient with no warning signs** (particularly when fever subsides); able to tolerate an adequate volume of oral fluids and pass urine at least once every 6 hours; near-normal blood counts and hematocrit. Patients can be sent home and reviewed for disease progression on a daily basis until they are out of critical period.
- ▀ **General measure/supportive care**
 - ▀ Prevention: avoid mosquito exposure and use mosquito repellent.
 - ▀ Tepid sponging if the patient still has high fever.
 - ▀ Oral fluids: Patients should be encouraged to rest & take oral fluids approximately 2.5L/24 hours for an adult. N.B. Oral rehydration products, fruit juices, & clear soups are better than water. Red- or brown-colored fluids should be avoided, as these may lead to confusion about the presence of hematemesis if the patient vomits.
- ▀ **Monitoring:**
 - ▀ Patients should be monitored for development of warning signs. An instruction leaflet outlining signs should be given to the patient, as well as advice to RETURN TO THE HOSPITAL IMMEDIATELY if any warning signs develop include abdominal pain, persistent vomiting, bleeding, lethargy/drowsiness, and breathing difficulty.
 - ▀ Complete blood count (CBC) tests should be performed on a daily basis.

1. Tab. Paracetamol 500mg (Calpol, Panadol) at dose 500mg to 1000mg orally every 6 hours when required. Maximum daily dose: 4000mg/day.
2. Syp. Multivitamins/appetizer (Lysovit, Leaderplex, Tresorix fort) x 10ml (2 teaspoonful) x twice daily
3. Tab. Folic acid 5mg (Folic acid) x once daily
4. Plenty of fluids/ORS therapy, coconut water (avoid excess plain water)

Note: Do not use NSAIDs (Aspirin, ibuprofen, diclofenac) to decrease the risk of gastritis and bleeding, particularly in patients with a predilection for hemorrhage or with abnormalities in platelets, liver function, or clotting factors. Glucocorticoids have not been shown to help. No existing antivirals are effective.

Avoid intra-muscular (IM) injection, tooth brushing, shaving and combing as risk of bleeding.

Avoid antiplatelet (aspirin/clopidogrel) and anticoagulants (Heparin/warfarin)



WHO GROUP-B (Dengue with developing warning signs) REQUIRE HOSPITAL ADMISSION

- Group-B with **ABSENT** warning signs → Follow WHO Group-A ± Maintain intravenous fluid (NS, RL) if required.
- Group-B with **POSITIVE** warning signs.
 - » Stabilize patients using ABCD&E approach.
 - » Establish large-bore intravenous (IV) access.
 - » Vitals monitoring: Check BP, PR, RR, Temperature and Check SpO₂ & Give high flow O₂ as appropriate.
 - » Send labs: CBC, (Thrombocytopenia 'platelets <100,000/mm³'), BUN/urea, creatinine, electrolytes (AKI/ARI), PT INR, LFTs, serum albumin, MP ICT, Dengue NS1 Ag & Dengue IgM + IgG serology, in severe cases LP
 - » Check hematocrit (HCT) level:
 1. If hematocrit (HCT) level increasing (> 45) → Give IV isotonic crystalloid (Normal saline, Ringer lactate) in stepwise manner initially at dose 5–7 ml/kg/hour for 1 to 2 hours, then 3–5 ml/kg for 2 to 4 hours.
 2. Recheck hematocrit (HCT) level and reassess clinical status of the patient:
 - ↳ If patient clinically stable and has no change or minimal change in hematocrit (HCT) level → continue isotonic crystalloid (Normal saline, Ringer lactate) at 2–3 ml/kg/hour for 2 to 4 hours → Recheck HCT and Reassess clinical status/hemodynamic stability of the patient.
 - ↳ If: adequate fluid intake, urine output and hematocrit (HCT) level decrease to baseline level or slightly below baseline level, but patient is clinically stable.
 - ↳ Then: reduce isotonic crystalloid (NS, RL).
 - ↳ OR If patient with worsening vital sign and rapidly increasing hematocrit (HCT) level → increase isotonic crystalloid (Normal saline, Ringer lactate) to 5–10 ml/kg/hour for 1 to 2 hours → Recheck HCT level and Re-assess clinical status of the patient.
 - ↳ If patient is improving → Reduce isotonic crystalloid (NS, RL) in stepwise manner. Reassess clinical status/hemodynamic stability of the patient before each change:
 1. Isotonic crystalloid (NS, RL) x 5–10 ml/kg/hour for 1 to 2 hours
 2. Isotonic crystalloid (NS, RL) x 3–5 ml/kg/hour for 2 to 4 hours
 3. Isotonic crystalloid (NS, RL) x 2–3 ml/kg/hour for 2 to 2 hours
 - ↳ OR If patient not improving & develops compensated/hypotensive shock → Follow WHO Group-C
- » For fever/analgesia: Paracetamol 1g/100ml IV infusion (Provas, Bofalgan) x TDS/QID (Maximum: 4g/day)
- » Gastroprotective: Inj. Omeprazole 40mg (Ruling, Risek) OR Inj. Esomeprazole 40mg (Esso, Nexum) x IV x OD
- » For Nausea/vomiting: Inj. Dimenhydrinate 50mg/ml (Gravinate) x IV x TDS
OR Inj. Metoclopramide 10mg/2ml (Metaclon) x IV x TDS (Caution: may causes Extra-pyramidal syndrome)
OR Inj. Ondansetron 8mg/2ml (Onset, Onseron) - Diluted in 50-100 ml 0.9% N/S over 15 minutes.
- » Inj. Neurobion 2ml/ampule x IV slow x OD
- » Consider platelets transfusion: if platelets count is ≤10,000 or there is any evidence of bleeding from any site with thrombocytopenia.



WHO GROUP-C (Dengue with established warning signs) REQUIRE EMERGENCY MEDICAL TREATMENT & SPECIALIST CARE WITH ICU INPUT

Follow WHO guideline: https://www.cdc.gov/dengue/resources/dengue-clinician-guide_508.pdf

BRUCELLOSIS

- Definition: Brucellosis is the most common zoonotic disease that can affect various organs, tissues, and systems. It is previously known as **Malta fever** or **Undulant fever**.
- Etiology: In humans it is caused by different species of brucella, a genus of gram-negative bacteria including *B. melitensis*, *B. abortus*, *B. suis*, and *B. canis* (and more rarely by *B. pinnipediae*, *B. cetaceae*, and *B. inopinata* BO1).
- Transmission: Ingestion of contaminated food, esp. raw meat, unpasteurized dairy products and contact with infected animals (cattle, sheep, goats, and pigs)
- Risk factors: occupational or recreational exposure to infected animals' products (e.g., farmers, veterinarians, hunters, slaughterhouse workers, laboratory personnel), ingestion of contaminated foods, inhalation of infected aerosols, Conjunctival contact with infected material and travel to an endemic area)
- Pathophysiology: *Brucella* spp. survive and replicate within macrophages of the reticuloendothelial system → formation of noncaseating granulomas

CLINICAL FEATURES

- Incubation period: 1–3 weeks
- General: Flu-like symptoms, night sweats, high potentially undulant fever, painful lymphadenopathy
- Localized infection (Focal disease)
 - » Osteoarticular infection (e.g., osteomyelitis, spondylitis): Arthralgias, joint swelling, tenderness, low back pain
 - » Genitourinary infection (epididymo-orchitis, pyelonephritis): Epididymal and testicular tenderness, flank pain
 - » Cardiac infection (e.g., endocarditis, myocarditis): Murmurs, friction rubs, tachycardia
 - » Neurologic manifestation (Neurobrucellosis): Meningoencephalitis, focal brain or cranial nerve lesions.

DIAGNOSTIC WORKUP

- CBC: anemia, neutropenia, thrombocytopenia). LFTs: mild elevation of AST/ALT.
- Serology: serum agglutination test (Rose Bengal test), ELISA for brucella → positive agglutination titer of ≥ 160
- Confirmatory test
 - » Blood culture OR CSF fluid culture OR bone marrow culture → Positive growth of *Brucella* species
 - » Tissue biopsy: Clinically affected organs and tissues can be biopsied, particularly lymph nodes, and liver, and occasionally Synovium → Histopathology: non-caseating granulomas.
- Culture medium for isolation: charcoal yeast extract agar (cysteine and iron buffered)
- X-ray of affected joint (small joint erosion, destruction, loss of space) & Chest X-ray (normal or pleural effusion)



UNCOMPLICATED BRUCELLA DISEASE (ACUTE WITHOUT FOCAL DISEASE)

1. Cap. Doxycycline 100mg (Vibramycin, Doxyn) x BD
2. PLUS Inj. Streptomycin 1g x IM, OD for 3 weeks (IM administration may be difficult/painful)
OR Inj. Gentamicin 40mg/ml x at dose 5mg/kg x IM/IV, OD for 7–10 days
OR Tab. Rifampicin 300mg (Lederrif, Rimactal) x per orally x Twice daily for 6 weeks
3. For fever/analgesia: Tab. Paracetamol 500mg (Calpol, Panadol) at dose 500 to 1000mg x TDS/QID
4. Syp. Multivitamins/appetizer (Lysovit, Leaderplex) x 10ml (2 teaspoonful) x Twice daily



COMPLICATED BRUCELLA DISEASE (FOCAL DISEASE)

1. Cap. Doxycycline 100mg (Vibramycin, Doxyn) x twice daily for at least 3–6 months
2. PLUS Tab. Rifampicin 300mg (Lederrif, Rimactal) x twice daily for at least 3–6 months.
3. PLUS Inj. Streptomycin 1g x IM, OD for 2 weeks
OR Inj. Gentamicin 40mg/ml x at dose 5mg/kg x IM/IV, OD for 7–10 days
OR FOR NEUROBRUCELOSIS Inj. Ceftriaxone (Oxidil, Rocephin) at dose 1–2g x IM/IV x OD, for 3–6 months



WEIL'S DISEASE (LEPTOSPIROSIS)

Epidemiology

- » Leptospirosis is the most common zoonotic disease worldwide and most common in the tropics.
- » **Low incidence in the USA (100–200 cases per year):** Half of these cases are reported in Hawaii.

» **Pathogen:** *Leptospira* (especially *L. interrogans*); a genus of gram-negative spirochete with hook-shaped ends

Route of infection

- » Contact with soil, food, and/or water contaminated with the urine of infected animals (most commonly rodents) → entry of *Leptospira* through skin/mucous membrane lesions.
- » **Occupational groups at risk:** Farmers, sewer workers and Water sports enthusiasts (surfers)

△ Weil's Disease

C/C:

Incubation time is 2–30 days.

Mild (anicteric) leptospirosis: Clinical manifestations during the early phase are due to bacteremia.

- » High fever, headache
- » Diarrhea, vomiting
- » **Conjunctival suffusion:** bilateral diffuse reddening of the conjunctivae without exudates
- » Photophobia and rashes
- » Myalgias; (especially in the calves and lower back)
- » Possibly aseptic meningitis → worsening headache and photophobia

Severe leptospirosis (Weil disease, icterohemorrhagic leptospirosis) → Clinical features are due to systemic spread and multiorgan involvement.

- » **Fever**
- » **Hepatitis** → hepatomegaly, jaundice, acute hepatic failure
- » **Acute kidney injury** (interstitial nephritis, acute tubular necrosis) → oliguria, hematuria
- » **Anemia, azotemia**
- » **Hemorrhagic diathesis**
 1. Purpura
 2. Pulmonary hemorrhage → hemoptysis
- » **Cardiac abnormalities**
 - Myocarditis & Pericarditis
 - Arrhythmia
 - Conductivity impairment

Microscopic agglutination test (MAT) is a gold standard investigation.

Treatment duration is typically 7 days.

Severe leptospirosis is associated with a high mortality rate

Antibiotic treatment may induce a **Jarisch-Herxheimer's reaction** specially penicillin

Diagnostic workup

- » **Dark-field microscopy of urine or blood;** samples (the thin *Leptospira* spirochetes cannot be visualized by light microscopy)
- » **Serological tests**
 - » Four-fold rise in the level of IgM titers within one month of the onset of symptoms
 - » **Microscopic agglutination test (MAT)**
 - Patient serum is incubated with *Leptospira* serovars, & titers are obtained for serovars that react with patient serum.
 - Positive one week after the onset of symptoms.
- » **PCR:** Detect leptospiral DNA in bodily fluids.
- » **Culture and sensitivity**
- » **CBC:** Leukocytosis (neutrophilic) & can show thrombocytopenia and anemia in Weil disease.
- » **Renal function tests:** elevated BUN in Weil disease
- » **Liver function tests (LFTs):** ↑ AST/ALT



TREATMENT OF MILD LEPTOSPIROSIS

- » **Antibiotics therapy:**
 - » **Cap. Doxycycline 100mg** (Doxyn, Vibramycin) x BD for 7 days
OR **Azithromycin 500mg** (Azomax, Azitma) x twice daily (BD) on day-1 then followed by 500mg OD for 3 days.
OR **Cap. Amoxicillin 500mg** (Amoxil, Zeemox) x I – I – I (TDS)
- » **Supportive therapy for other symptoms:** analgesia, antiemetic



TREATMENT OF SEVERE LEPTOSPIROSIS

- » **Treatment of underlying cause:** cough, fever, pain, vomiting
- » **IV fluid and electrolyte correction**
- » **Supportive therapy for multiorgan failure**
 1. **Inj. Ceftriaxone 1g** (Oxidil, Rocephin) x once daily x IV for 7 days
OR **Inj. Penicillin 1.5MU** x every 6-hourly x IV for 7 days
OR **Inj. Cefotaxime 1g** (Claforan) every 6-hourly for 7 days
 2. **With nausea &/or vomiting:**
 - » **Tab. Domperidone 10mg** (Motilium, Domel) x TDS
 - » OR **Inj. Metoclopramide 10mg/2ml** (Metaclon) x IV x TDS

SCHISTOSOMIASIS

- Risk Factors: Skin exposure to contaminated fresh water, travel to endemic area, occupational exposure
- Etio-Pathogenesis: Schistosomes (parasitic trematodes or flukes of the genus *Schistosoma*) → Infected humans (definitive host) excrete schistosome eggs in urine or feces.
 - » *Schistosoma mansoni*: Africa, South America, and the Caribbean
 - » *Schistosoma haematobium*: Africa and the Middle East
 - » *Schistosoma japonicum*: China and Southeast Asia

Clinical features

Clinical features depend on the stage, schistosome type, and infected organs.

- Local reaction (swimmer's itch or cercarial dermatitis): pruritic maculopapular rash at the point of entry of cercaria into human skin
- Acute schistosomiasis syndrome (Katayama fever)
 - » Serum sickness-like disease: immune complex formation of antigens released from eggs and/or adult worms with host antibodies.
 - » Incubation period: 3–8 weeks
 - » Clinical features: Fever, fatigue, cough, myalgia, angioedema
 - » Patients usually spontaneously recover after 2–10 weeks.
- Chronic schistosomiasis: Deposition of eggs leads to chronic inflammation and granuloma formation.

SUBTYPE	PATHOGEN	CLINICAL FEATURES
Genitourinary schistosomiasis	» <i>S. haematobium</i>	» Hematuria, dysuria » Complications (especially with chronic infection) ▪ Squamous cell carcinoma of bladder (may cause painless hematuria) ▪ Infertility (particularly in women) ▪ Bladder neck obstruction and hydronephrosis
Hepatosplenic schistosomiasis	» <i>S. mansoni</i> » <i>S. japonicum</i> » <i>S. haematobium</i> (less common)	» Children and adolescents: hepatosplenomegaly » Adults with chronic infection: periportal fibrosis & portal hypertension » Complications: pulmonary schistosomiasis, neuroschistosomiasis
Intestinal schistosomiasis		» Diarrhea, Abdominal pain, Intestinal bleeding, bowel strictures
Pulmonary schistosomiasis	» <i>S. mansoni</i>	» Pulmonary hypertension and cor pulmonale
Neuroschistosomiasis	» <i>S. japonicum</i> » <i>S. haematobium</i>	» Headache, Transverse myelitis » Sensory and motor deficits and Epilepsy

DIAGNOSTICS WORKUP

- CBC (mild anemia, eosinophilia), LFTs (normal, except in ESLD), Blood culture (Negative), Urinalysis (RBCs, Protein, Bacteria)
- Serology test: ELISA – *Schistosoma* → detection of antibodies against parasite antigens
- Definitive diagnosis (gold standard): stool or urine microscopy → direct visualization of schistosome eggs
- Egg morphology is indicative of *Schistosoma* subtype:
 1. *Schistosoma Mansoni*: Eggs have a prominent lateral spine.
 2. *Schistosoma Haematobium*: Eggs have a prominent terminal spine.
 3. *Schistosoma Japonicum*: Eggs have a miniscule lateral spine.
- Detection of antigens in urine/stool is sometimes used to measure treatment efficacy.
- US abdomen: Characteristic changes may be observed in bladder and kidneys or in the portal veins and liver parenchyma.
- CT scan abdomen/MRI abdomen: Useful in diagnosis and subsequent follow-up of treatment.
- Chest x-ray & CT chest (Indicated for Respiratory symptoms) & MRI Brain & spine (Indicated for neurologic symptoms)



TREATMENT OF SCHISTOSOMIASIS

- Acute schistosomiasis syndrome
 - » Corticosteroids: Tab. Prednisolone 5mg (Deltacortril) at dose 1mg/kg/day orally for 1 week, followed by 0.5 mg/kg/day for 1 week, followed by 0.25 mg/kg/day for 1 week; start course one day before Praziquantel
 - » Tab. Praziquantel 600mg (Distoside, Biltricide) should only be given as dose below after acute symptoms have resolved.
- Chronic schistosomiasis: Tab. Praziquantel 600mg (Distoside, Biltricide) x 20mg/kg x BD/TDS (depending on species) for 1 day
 - Dosage: a single dose of 40 mg/kg for *S. haematobium*, *S. mansoni*, or *S. intercalatum* infections; 2 divided doses of 60 mg/kg for *S. japonicum* or *S. mekongi* infections), which is the preferred treatment, is effective in 70 to 100% of cases.
 - However, a second dose Tab. Praziquantel can be given 6 to 12 weeks later, particularly in patients with eosinophilia, high antibody titers, or persistent symptoms. Despite treatment, 5 to 20% of patients develop significant hepatic fibrosis.
- Oral Antihistamines for Pruritus: Tab. Cetirizine 10mg, OR Tab. Levocetirizine 5mg x once or twice daily

LEISHMANIASIS

- Definition: Leishmaniasis is a vector-borne parasitic disease caused by protozoans of the *Leishmania* genus, which are transmitted by infected **phlebotomine sand flies**. Depending on the parasite subtype and the strength of the host's immune system, the disease manifests in a cutaneous leishmaniasis or visceral leishmaniasis.
 - Cutaneous leishmaniasis is characterized by skin ulcers.
 - Visceral leishmaniasis (**kala-azar in Urdu = "black fever"**), which presents darkening of the skin, fever, weight loss, hepatosplenomegaly, and immunosuppression.
- Pathogen: *Leishmania donovani* (protozoan)
- Transmission: Transmitted by bite of an infected **phlebotomine sandfly**
- Pathogenesis: The obligate intracellular parasite is transmitted to mammals via the sandfly → 1. The parasite binds to macrophages of the reticuloendothelial system, 2. Coinfection with HIV/AIDS.
- Strong risk factors: High exposure to sandfly bites, poverty, ownership of domestic animals, immunosuppression



CUTANEOUS LEISHMANIASIS (CL)

Clinical features	Diagnostic workup
- Localized cutaneous leishmaniasis (CL) - Incubation period: weeks to months - Manifestation: solitary or multiple reddish macules/papules around the sandfly bite that quickly increase in size and develop central ulceration - Mucosal leishmaniasis - Some <i>Leishmania</i> subtypes (e.g., <i>L. braziliensis</i>, <i>L. guyanensis</i>, <i>L. panamensis</i>) cause mucosal leishmaniasis, which can develop months to years after cutaneous leishmaniasis that was not treated properly. - Manifestation: commonly affects the nasopharynx (mucosal bleeding, nasal blockage)	- Detection of the pathogen in skin biopsy - Microscopy of specimen/tissue biopsy: - Biopsy aspirates, smears, scrapings, and skin slit smears are used. - Results: macrophages that contain amastigotes, the intracellular, non-motile form of <i>Leishmania</i> (appear as ovoid inclusions) - PCR: <i>Leishmania</i> DNA - Tissue Culture (Novy-Nicolle-McNeal medium) → Promastigote forms of the <i>Leishmania</i> species in culture media



TREATMENT OF CUTANEOUS LEISHMANIASIS (CL)

- Uncomplicated disease (Simple CL): No immunosuppression, small lesions, no mucosal involvement
 - Watchful waiting is preferred.
 - Wound management: Care should be taken to ensure proper wound management including washing the ulcer(s) and applying barrier ointment. The presence of warmth, redness, pain, and/or purulent discharge should prompt the evaluation and management of a secondary bacterial infection.
 - Local therapy includes cryotherapy, thermotherapy, and topical or intralesional medications. Before any local therapy is started, any crust should be removed, if present.
 - Azoles antifungal: Fluconazole, ketoconazole, itraconazole are options where local therapies are not available
 - Cryotherapy with liquid nitrogen: it involves freezing the lesion and surrounding 1 to 2mm of healthy skin with liquid nitrogen until it is white in appearance, allowing the area to thaw, and freeze again.
- The IDSA/ASTMH guidelines recommend a cryotherapy session every 3 weeks up to 3 times total.
- Per lesion efficacy of cryotherapy is same as intralesional antimonial compounds.
- Adverse effects: transient pain, redness as well as hypopigmentation.
- Thermotherapy: utilizes heat administered to the lesion(s), often in a single treatment, resulting in a 2nd degree burn & requiring local anesthesia. It is equivalent to systemic antimonial therapy but with fewer adverse effects
- Topical paromomycin: the best studied topical medication for the treatment of cutaneous leishmaniasis (CL)
 - Paromomycin may be used alone or in combination with methylbenzethonium chloride, urea, or gentamicin.
- Complicated disease (Complex CL): Mucosal involvement, numerous lesions, immunosuppression
 - Same as visceral leishmaniasis → antileishmanial drug (explained below)



VISCERAL LEISHMANIASIS (VL)

Clinical features

- Incubation period: 2 to 6 months
- Many patients are asymptomatic.
- Kala-azar ('black fever' in reference to the darkening of the skin it can cause)
 - » Usually insidious progression
 - » Flu-like symptoms: fatigue, cough, headache, anorexia.
 - » Prolonged fevers (weeks or months) – double quotidian
 - » Weight loss
 - » Lymphadenopathy
 - » Hepato-splenomegaly
 - » Ascites and edema
 - » Skin darkening: Possible darkened or gray skin color (especially on the palms and soles)
 - » Immunosuppression may lead to secondary bacterial infections in advanced disease

Diagnostic approach

- CBC: anemia, leukopenia, neutropenia, eosinopenia, thrombocytopenia (Pancytopenia)
- LFTs: variable; may be elevated.
- BUN & creatinine level: normal or elevated
- Detection of pathogen:
 - » Microscopy of specimen/tissue biopsy:
 - ↳ Specimen can be obtained by aspiration of splenic tissue (discouraged due to risk of fatal hemorrhage), lymph node, bone marrow or liver tissue.
 - ↳ Results: Amastigotes form of Leishmania species in macrophages or monocytes
 - » PCR: Leishmania DNA
- Serology: Positive for Leishmania antibodies
- Serum HIV testing: may be positive or negative



TREATMENT OF VISCERAL LEISHMANIASIS (VL)

- Supportive care: management must address frequent complications such as volume depletion, malnutrition, anemia, and concomitant bacterial infections (e.g., pneumonia) or parasitic infections (e.g., malaria).
- 1. Amphotericin B
 - ↳ Liposomal Amphotericin-B at dose 3 mg/kg/day IV on days 1–5, 14, and 21. Simpler regimens that have shown good efficacy include four doses of 5 mg/kg over 4–10 days and a single dose of 15 mg/kg.
 - ↳ Amphotericin B lipid emulsion as single infusion is more affordable than liposomal preparations, showed excellent efficacy, albeit lower than that of the liposomal formulation.
 - ↳ Conventional amphotericin B deoxycholate at dose 1mg/kg/day for 15–20 days or 0.5–1mg/kg every second day for up to 8 weeks x slow IV infusion (much less expensive, is also highly effective but with more toxicity).
- 2. Pentavalent antimonials
 - ↳ Sodium stibogluconate (Pentostam) at dose 20 mg/kg once daily IV (preferred) or IM for 28 days.
 - ↳ OR Meglumine antimoniate (Glucantime) at dose 20mg Sb⁺/kg/day for 28 days.
- 3. Cap. Miltefosine 50mg (Fosine, Visral) at dose 2.5 mg/kg, orally daily in two divided doses for 28 days.
- 4. Inj. Paromomycin at dose 11mg/kg/day IM for 21 days was shown to be similarly efficacious to amphotericin-B.
- Combination therapy: The use of drug combinations to improve treatment efficacy, shorten treatment courses, and reduce the selection of resistant parasites has been actively studied.
 - A. In India, compared with a standard 30-day (treatment on alternate days) course of amphotericin, noninferior efficacy and decreased adverse events were seen with a single dose of liposomal amphotericin plus a 14-day course of miltefosine, a single dose of liposomal amphotericin plus a 10-day course of paromomycin (15 mg/kg/day IM), or a 10-day course of miltefosine plus paromomycin.
 - B. In East Africa, the efficacy of amphotericin B is lower than in Asia, and the standard treatment is a combination of sodium stibogluconate (20 mg/kg/day IV) plus paromomycin (15 mg/kg/day IM) for 17 days, with shows excellent efficacy; liposomal amphotericin B may be considered in older adults or pregnant women due to toxicity concerns.

SCRUB TYPHUS (TICK TYPHUS)

- Definition: an exanthematous typhus fever caused by *Orientia tsutsugamushi*
- Epidemiology: occurs mainly in central, eastern, and southeast Asia, as well as northern Australia & South Pacific
- Transmission: via vector, *Trombicula mites* larvae (chiggers) from rodents

CLINICAL FEATURES

- Incubation period: 7-10 days
- Constitutional symptoms: High fever, severe headache, cough, and anorexia
- Myalgias, arthralgia
- Maculopapular rash
- Eschar at site of tick bite is pathognomonic.
- Lymphadenopathy
- Relative bradycardia despite fever
- Meningitis (seizures, ALOS, neck rigidity) → multiorgan dysfunction syndrome (MODS).

DIAGNOSTIC WORKUP

- CBC: Low platelet count
- BUN & creatinine: ↑ creatinine
- LFTs: ↑ ALT and AST, ↑ bilirubin
- Indirect fluorescent antibody (IFA) test: BEST
 - Four-fold rise in rickettsial antibodies
- Weil-Felix test: Positive Weil-Felix reaction
- Other tests: indirect immunoperoxidase assay, serological test (ELISA), PCR, blood culture, CSF analysis, Chest x-ray, if required.



TREATMENT OF SCRUB TYPHUS (TICK TYPHUS)

- Cap. Doxycycline 100mg (Vibramycin, Doxyn, wellcodox) 1-0-1 (BD) x Twice daily for 7-14 days. (Ref: NIH/NCBI/NLM)
 - Contraindication: children, pregnancy, breast-feeding
 - Alternative: Cap. Azithromycin 500mg x OD for 5 days.
 - Tab. Rifampin 300mg (Lederrif) x 600-900mg x OD, 7 days
- Tab. Paracetamol (Panadol, Calpol, Febrol) 1-1-1 (1 x TDS) OR 2-2-2 (2 x TDS)
 - Dose: 500mg-1000mg (1-2 tablets) x TDS/QID, Max. 4g/day
- Cough suppressants for symptomatic relief:
 - Syp. Hydrillin x 2 Teaspoonful (10ml) x TDS
 - OR Syp. Corex-D x 2 Teaspoonful (10ml) x TDS
- Appetite stimulant/multivitamins:
 - Syp. Trimetabol x 10ml x 30 min before meals x BD
 - OR Syp. Tresorix fort x 10ml x 30 min before meals x BD
- Referral to tertiary care: Scrub typhus meningitis/ Meningo-encephalitis (more severe form), seen in a setting of MODS.

EPIDEMIC TYPHUS

- Definition: An exanthematous typhus fever caused by *Rickettsia prowazekii*.
- Epidemiology: Occurs mainly in central & eastern Africa, central and South America, and Asia. Rare in USA,
- Transmission: via vector → Direct contact with persons and/or feces of infected human body lice

CLINICAL FEATURES

- Constitutional symptoms: abrupt onset of high fever, severe headache, cough, and anorexia
- Abdominal pain, Myalgia
- After 4-5 days: maculopapular or petechial rash that spreads from the trunk to the extremities.
- Possibly CNS symptoms: confusion, coma, seizures
- Brill-Zinsser disease (Recrudescence infection): Reactivation of latent infection with *R. prowazekii* that occurs months to years after the initial infection due to stress or immunosuppression.

DIAGNOSTIC WORKUP

- CBC: Low platelet count
- BUN & creatinine: ↑ BUN
- LFTs: ↑ ALT and AST, ↑ bilirubin
- Indirect fluorescent antibody (IFA) test: BEST
 - Four-fold rise in rickettsial antibodies
- Weil-Felix test: Positive Weil-Felix reaction
- Other tests: Serological test (ELISA), PCR, blood culture, CSF analysis, Chest x-ray, if required.



- Cap. Doxycycline 100mg (Vibramycin, Doxyn) 1-0-1 (BD) for 7-10 days or until the patient improves.
 - Alternative: Chloramphenicol 500 mg orally or IV four times daily for 7-10 days. (Ref: NIH/NCBI/NLM)
 - Macrolides are not recommended therapy.
- Tab. Paracetamol (Panadol, Calpol, Febrol) 1-1-1 (1 x TDS) OR 2-2-2 (2 x TDS)
 - Dose: 500mg-1000mg (1-2 tablets) x TDS/QID, Max. 4g/day
- Cough suppressants for symptomatic relief:
 - Syp. Hydrillin x 2 Teaspoonful (10ml) x TDS
 - OR Syp. Corex-D x 2 Teaspoonful (10ml) x TDS
- Appetite stimulant/multivitamins:
 - Syp. Trimetabol x 10ml x 30 min before meals x BD
 - OR Syp. Tresorix fort x 10ml x 30 min before meals x BD

Gold standard test is IFA: is used as a reference technique in most research labs for serodiagnosis of rickettsiosis, to determine IgG &/or IgM. IFA identification of specific IgM antibodies in several species of *Rickettsia* provides strong evidence of recent active infection

ENDEMIC TYPHUS (MURINE TYPHUS)

- Definition: an exanthematous typhus fever caused by *Rickettsia typhi*
- Epidemiology: occurs worldwide, mainly in warm coastal regions, southern USA
- Transmission: via vector (exposure to infected rat and cat fleas)

CLINICAL FEATURES

- Incubation period: 8–16 days
- Constitutional symptoms: Fever, severe headache, malaise, and anorexia
- Maculopapular or petechial rash erupts on the trunk; and spreads to the extremities (palms and soles are spared).
- No eschar (scab at site of flea bite)
- Relative bradycardia, altered mental state.

DIAGNOSTIC WORKUP

- CBC: ↑ or ↓ WBCs, ↓ platelet count, & anemia
- BUN & creatinine: ↑ BUN. Serum albumin: ↓
- LFTs: ALT and AST (3–5 times than ULN)
- Indirect fluorescent antibody (IFA) test: BEST
 - Four-fold rise in rickettsial antibodies
- Weil-Felix test: Positive Weil-Felix reaction
- Other tests: Serological test (ELISA), PCR, blood culture, CSF analysis, Chest x-ray, if required.

Rx

- Cap. Doxycycline 100mg (Vibramycin, Doxyn)
1 – 0 – 1 (BD) for 7–10 days
- Tab. Paracetamol (Panadol, Calpol, Febrol)
1 – 1 – 1 (1 x TDS) OR 2 – 2 – 2 (2 x TDS)
Dose: 500mg–1000mg (1–2 tab.) x TDS/QID, Max. 4g/day
- Cough suppressants for symptomatic relief:
 - Syp. Hydrillin x 2 Teaspoonful (10ml) x TDS
 - OR Syp. Corex-D x 2 Teaspoonful (10ml) x TDS
 - OR Syp. Pulmonol x 2 Teaspoonful (10ml) x TDS
- Appetite stimulant/multivitamins:
 - Syp. Trimetabol x 10ml x 30 min before meals x BD
 - OR Syp. Tresorix fort x 10ml x 30 min before meals x BD



ROCKY MOUNTAIN SPOTTED FEVER

- Definition: an infection caused by *Rickettsia rickettsii* & carried by the American dog tick (*Dermacentor variabilis*). The organism invades the endothelial lining of capillaries and causes small vessel vasculitis.
- Epidemiology: occurs worldwide, mainly in warm coastal regions, southern USA
- Transmission: transmitted by ixodid ticks.

CLINICAL FEATURES

- Constitutional symptoms: Fever with chills, headache, myalgia, and anorexia.
- Maculopapular rash: The characteristic rash is initially macular (beginning on the wrists and ankles) but becomes petechial/purpuric as it spreads centrally.
- No eschars.
- ALOS (reduced GCS) or DIC (in severe cases).

DIAGNOSTIC WORKUP

- CBC: normal WBCs, low platelets, anemia
- LFTs: mildly raised AST &/or ALT.
- Serum electrolytes: ↓ sodium level
- Confirmatory test indicated in all patients.
 - Indirect fluorescent antibody (IFA) test (gold standard): four-fold increase in IgG-specific antibodies
 - PCR: detection of *R. rickettsii* DNA in a skin biopsy specimen or acute phase whole blood specimen
 - Immunohistochemical staining of *R. rickettsii* in a skin biopsy specimen.
- Lumbar puncture in suspected meningitis
- Chest x-ray and ECG

Rx

- Cap. Doxycycline 100mg (Vibramycin, Doxyn)
1 – 0 – 1 (BD) twice daily for 5–7 days.
- Tab. Paracetamol (Panadol, Calpol, Febrol)
1 – 1 – 1 (1 x TDS) OR 2 – 2 – 2 (2 x TDS)
Dose: 500mg–1000mg (1–2 tablets) x TDS/QID, Max. 4g/day
- Cough suppressants for symptomatic relief:
 - Syp. Hydrillin x 2 Teaspoonful (10ml) x TDS
 - OR Syp. Corex-D x 2 Teaspoonful (10ml) x TDS
- Appetite stimulant/multivitamins:
 - Syp. Trimetabol x 10ml x 30 min before meals x BD
 - OR Syp. Tresorix fort x 10ml x 30 min before meals x BD

Prognosis

- If treated within the first 5 days, patients typically fully recover without hospitalization.
- If treated after the first 5 days, symptoms are more severe and often require hospitalization. There is also a greater risk of long-term consequences of ischemia (e.g., amputations, paralysis, hearing loss, intellectual disability).

COXIELLA BURNETII INFECTIONS (Q-FEVER)

Name: _____ Age: _____ Sex: _____ Date: _____
 Temperature: _____ B.P: _____ Pulse: _____ Resp. Rate: _____

Agents: Obligate intracellular (sub type of Rickettsia)

Risk factors: Exposure to infected animals (cattle, sheep, and goats), Aerosol transmission, occupational exposure to animal products (farmers, veterinarians, and abattoir workers) and immunosuppression

Clinical features

- » Present as atypical pneumonia: slow onset, Low grade fever, dry cough and mild dyspnea.
- » Extra-Pulmonary Symptoms: severe headache, arthralgia, myalgia, nausea, vomiting, diarrhea, hepatitis, chronic fatigue and seizures, coma.
- » On auscultation: inspiratory crackles, wheezing, and coarse crepitation.
- » Special features: Infective endocarditis (Fever + murmur)

Diagnostic workup

- » Chest X-ray: Patchy or diffuse interstitial infiltrates (Bronchopneumonia)
- » CBC: Normal or raised WBC, low platelets.
- » LFTs: abnormal/raised. CRP/ESR: Increases
- » Echocardiography: suspected endocarditis from chronic Q fever → vegetation on valves, most commonly mitral valve
- » Best initial test: Serology via IFA (Anti-Coxiella IgM) = Acute infection: phase II antigen IgM titer $\geq 1:50$ and phase II antigen IgG $\geq 1:200$, or seroconversion; persistent focalized infection: phase I antigen IgG $\geq 1:800$ and low or absent phase II antigen IgM (Repeat serological test at 3rd and then 6th months)
- » If IFA -ve, do PCR of serum or tissue samples.
- » Blood cultures are often negative.

Rx

TREATMENT FOR COXIELLA BURNETII (Q-FEVER)

1. Cap. Doxycycline 100mg (Vibramycin, Doxyn)
 1-0-1 (BD) for 14 days.
 Alternative: Azithromycin 500mg x OD
2. Tab. Paracetamol (Panadol, Calpol, Febrol)
 1-1-1 (1 x TDS) OR 2-2-2 (2 x TDS)
 Dose: 500mg-1000mg (1-2 tablets) x TDS/QID, Max. 4g/day
3. Cough suppressants for symptomatic relief:
 ↳ Syp. Hydrillin x 2 Teaspoonful (10ml) x TDS
 ↳ OR Syp. Corex-D x 2 Teaspoonful (10ml) x TDS
4. Appetite stimulant/multivitamins:
 ↳ Syp. Trimetabol x 10ml x 30 min before meals x BD
 ↳ OR Syp. Tresorix fort x 10ml x 30min before meals x BD

Treatment for Chronic stages:

- » Cap. Doxycycline 100mg (Vibramycin) x BD
 PLUS Tab. Hydroxychloroquine 200mg (HCQ, Plaquin-H)
 1-1-1 (TDS) x Three times a day for atleast 18 months
 Alternative: Rifampin PLUS doxycycline or ciprofloxacin

Treatment for pregnant women:

- » Tab. Trimethoprim/sulfamethoxazole (Septran DS) →
 Outcome → may reduce fetal death.
 Duration: until the end of the 7 months.

TRICHURIASIS (WHIPWORM)

Name: _____ Age: _____ Sex: _____ Date: _____
 Temperature: _____ B.P: _____ Pulse: _____ Resp. Rate: _____

Etiology: Trichuris trichiura (Human whipworms are nematodes).

Transmission: Fecal-oral route

CLINICAL FEATURES

- » Most persons with infection are asymptomatic.
- » In heavy infections: abdominal pain, distension, diarrhea, nausea, vomiting, iron deficiency anemia, growth retardation, swelling of intestine, trichuris dysentery, IBD, bloody diarrhea and rectal prolapse due to tenesmus.

DIAGNOSTIC WORKUP

- » CBC: Eosinophilia, anemia
- » Microscopic examination of stool for eggs
- » Concentration technique can be used for light infections.

Rx

TREATMENT OF TRICHURIASIS

- » Tab. Mebendazole 100mg (Vermox) x BD for 3 days
 OR Tab. Albendazole 200mg (Zentel) x BD for 3 days
 Dosage: for 1-3 days for light infections or 3-7 days for heavy infections.
- » OR Tab. ivermectin 6mg (Ivermectin) at dose 200 mcg/kg orally once daily for 3 days
- » OR Oxantel pamoate (one dose of 15-30 mg/kg)

FISH TAPEWORM INFECTION (DIPHYLLOBOTHRIUM LATUM)

Name:	Age:	Sex:	Date:
Temperature:	B.P:	Pulse:	Resp. Rate:
Etiology: <i>Diphyllobothrium latum</i> (Diphyllobothriasis or a fish tapeworm)			
Risk factors: living on farms, poor hygiene, eating or handling undercooked meat, ingestion of contaminated water.			
Transmission: consumption of raw or undercooked freshwater fish containing larvae			

CLINICAL FEATURES	DIAGNOSTIC WORKUP
- Usually asymptomatic. Worms segmental in stool - Prolonged infection leads to vitamin B12 deficiency anemia and peripheral neuropathy: Fish tapeworms compete with the host for dietary vitamin B12 in the intestine → anemia (fatigue, pallor), tingling, numbness, pin-&-needle sensation, and coldness (especially in lower limb, &/or CNS symptoms (raised ICP, fits).	- CBC: Eosinophilia and megaloblastic anemia: ↓Hb, ↑MCV & hypersegmented neutrophil - Serum vitamin B12 level - Stool examination for eggs or proglottids (i.e., segments of adult tapeworms) - Ultrasound abdomen & CT head if indicated

Rx

TREATMENT OF DIPHYLLOBOTHRIUM LATUM

- Tab. Praziquantel 600mg at dose 5-10 mg/kg per orally as a single dose
- With megaloblastic anemia: Supplementation with Vitamin B12 and folic acid – Hematology section
- Treatment of CNS involvement:
 - If raised ICP consult with neurosurgery for further evolution.
 - Control of seizures/fits (Anticonvulsants)
 - Concurrent corticosteroid (IV dexamethasone) therapy can help to control brain edema.

HOOKWORM INFECTIONS (ANCYLOSTOMA DUODENALE)

Name:	Age:	Sex:	Date:
Temperature:	B.P:	Pulse:	Resp. Rate:
Etiology: <i>Ancylostoma duodenale</i> and <i>Necator americanus</i> (ANCYLOSTOMIASIS; NECATORIASIS)			
Risk factors: Recent travels to or residence an endemic area, walking bare foot, sunbathing or contaminated beach.			
Transmission: Percutaneous penetration of larvae (primarily via the feet, e.g., while walking on a beach)			

CLINICAL FEATURES	DIAGNOSTIC WORKUP
- Most persons with infection are asymptomatic. - Transient pruritic maculopapular rash (ground itch) may occur at the site of larval penetration, usually in previously sensitized persons. - Lung's involvement during larva migration: Dry cough, wheezing, Loeffler syndrome - Gastrointestinal symptoms: epigastric pain, anorexia, nausea, vomiting, diarrhea. - chronically infected with large worm burdens may have abdominal pain, anorexia, diarrhea, and findings of marked iron deficiency anemia and protein malnutrition. - Microcytic anemia: Lead to pallor, weakness, dyspnea, palpitation, and heart failure - Protein loss can lead to hypoalbuminemia, edema, and ascites.	- CBC: Microcytic anemia and Eosinophilia. - Stool examination for eggs or worms. - Occult blood in the stool - Serum albumin: ↓ - Skin scrapings or biopsy

Rx

TREATMENT OF ANCYLOSTOMA DUODENALE

- FOR HUMAN HOOKWORMS:
 - Tab. Albendazole 200mg (Zentel) x 2 tablets (400mg) per orally once.
 - OR Tab. Mebendazole 500mg (Vermox) x One tablet per orally once.
 - OR Tab. Mebendazole 100mg (Vermox) x Twice daily (BD) for 3 days.
 - OR Syp. pyrantel pamoate 250mg/5ml (Combantrin) at dose 11 mg/kg (up to a max: 1g) PO, OD for 3 days.
 - OR Tab. Levamisole 40mg (Ketress) at dose 2.5-10mg/kg or 300-600mg as single dose. May repeat after week.
- WITH ANEMIA: should be treated with iron supplements and, for severe symptomatic anemia, blood transfusion.

ENTEROBIASIS (PINWORM)

- **Etiology:** *Enterobius vermicularis* (pinworm) → Pinworms are nematodes
- **Transmission:** Person-to-person via ingestion of eggs after contact with the hands or perianal region of an infected individual, food or fomites that have been contaminated by an infected individual, or infected bedding or clothing

CLINICAL FEATURES

- Most common symptoms nocturnal perianal pruritus (Anal pruritus at night)
- Insomnia, restlessness, enuresis and Vulvovaginitis are common in children.
- Perianal scratching may result in excoriation and impetigo.
- Occasionally, symptoms of intestinal infection (i.e., nausea, vomiting, and abdominal pain which may become severe enough to mimic appendicitis)

DIAGNOSTIC WORKUP

- **Tape test:** Microscopic detection of oval eggs (ova) &/or pinworms on tape that has been pressed against the perianal region.
- Can be an incidental finding on endoscopy.

Rx

TREATMENT OF ENTEROBIASIS (PINWORM)

- **Tab. Albendazole 200mg (Zentel)** x 2 tablets orally once.
- **OR Tab. Mebendazole 100mg (Vermox)** x Orally once
- **OR Syp. Pyrantel pamoate 250mg/5ml (Combantrin)** x at dose 11mg/kg per orally once. (Maximum: 1g).
- **Drug of choice in pregnancy:** Pyrantel pamoate. Should only be administered if pregnancy is compromised (e.g., weight loss, sleeplessness). Should not be started until the 3rd trimester, after which the risk to fetus is likely to be low.
- **The dose is repeated in 2 weeks due to frequent reinfection.** Other family members with infection should be treated concurrently, and treatment of all close contacts may be appropriate when rates of reinfection are high in family, school, or institutional settings. Standard hand washing and hygiene practices are helpful in limiting spread. Perianal scratching should be discouraged. Washing of clothes and bedding should kill pinworm eggs

ASCARIASIS (GIANT ROUNDWORM)

- **Etiology:** *Ascaris lumbricoides* (giant roundworm) → *Ascaris* are nematodes. Its commonest intestinal helminths.
- **Transmission:** Fecal-oral (infection occurs in the larval state following the consumption of contaminated food, especially raw vegetables that have been contaminated by human waste used as a fertilizer)

Clinical features

- Most persons are asymptomatic. symptoms develop during migration of worms through the lungs, with fever, nonproductive cough, chest pain, dyspnea, and eosinophilia, occasionally with eosinophilic pneumonia.
- **Early symptoms**
 - » Transient dry cough, blood-tinged sputum, wheezing
 - » **Loeffler syndrome:** Accumulation of eosinophils in the lungs due to certain infections (usually parasites) or allergic reactions to drugs. Symptoms are usually mild and resolve spontaneously.
- **Late symptoms:** anorexia, abdominal discomfort, nausea, vomiting, and diarrhea
- **Adult worms** may also migrate and be coughed up, be vomited, or may emerge through the nose or anus. They may also migrate into the common bile duct, pancreatic duct, appendix, and other sites, which may lead to cholangitis, cholecystitis, pyogenic liver abscess, pancreatitis, obstructive jaundice, or appendicitis. With very heavy infestations, masses of worms may cause intestinal obstruction, volvulus, intussusception, or death.

Diagnostic workup

- **CBC:** shows eosinophilia → marked during worm migration but may be absent during intestinal infection.
- **Confirmatory test:** Stool samples show the presence of worms or visible oval eggs with a knobby appearance under the microscope.

Rx

TREATMENT OF ASCARIASIS

- **Tab. Albendazole 200mg (Zentel)** x 2 tablets orally once.
- **OR Tab. Mebendazole 500mg (Vermox)** x One tablet once
- **OR Tab. Mebendazole 100mg (Vermox)** x Twice daily for 3 days.
- **OR Syp. Pyrantel pamoate 250mg/5ml (Combantrin)** x at dose 11mg/kg per orally once. (Maximum: 1g).
- **Tab. Ivermectin 6mg (Ivermectin)** at dose 200 mcg/kg, per orally once. Alternative (but not in children <35 kg or pregnant women)
- **During pregnancy:** Pyrantel pamoate

CUTANEOUS LARVA MIGRANS (CREEPING ERUPTION)

- ✓ Cutaneous larva migrans (CLM), also known as creeping eruption or sandworm disease, is a skin infection caused by hookworm larvae that migrate into the human epidermis/skin. Most commonly due to the dog hookworm *Ancylostoma caninum* and the cat hookworm *Ancylostoma braziliense*.
- ✓ Risk factors: recent travel to or residence in an endemic area, walking barefoot on a beach.
- ✓ Transmission: percutaneous penetration of larvae (primarily via the feet, e.g., while walking on a beach)

CLINICAL FEATURES

- ✓ At entry site: intensely pruritus, erythematous, maculopapular rash, develop, usually on the feet or hands.
- ✓ Followed within a few days by **serpiginous tracks marks** (cutaneous lesion with a progressive, creeping, snake-like border) during the parasite representing larval tracks, which may travel several millimeters per day.
- ✓ Several tracks may be present. The process may continue for weeks, with lesions becoming vesiculated, encrusted, or secondarily infected. Systemic symptoms and eosinophilia are uncommon.
- ✓ Diagnosis: The diagnosis is based on the characteristic appearance of the lesions. Biopsy is usually not indicated.

Rx**TREATMENT OF CUTANEOUS LARVA MIGRANS**

- ✓ Self-limited, without treatment, the larvae eventually die and are absorbed. Mild cases do not require treatment.
- ✓ Thiabendazole (10% aqueous suspension) can be applied topically three times daily (TDS) for 5 or more days.
- ✓ Tab. Albendazole 200mg (Zentel) 2 tablets (400 mg) orally once or twice daily for 3–5 days.
- ✓ OR Tab. Ivermectin 6mg (Ivermectin) at dose 200 mcg/kg orally, once, is highly effective

**LYMPHATIC FILARIASIS**

- ✓ Lymphatic filariasis is caused by filarial nematodes: *Wuchereria bancrofti* (responsible for most cases of lymphatic filariasis worldwide), *Brugia malayi*, & *Brugia timori* in Asia, and is among the most important parasitic diseases of man.
- ✓ Transmission: Female mosquito bite (*Aedes*, *Mansonia*, *Anopheles*, and *Culex*)

CLINICAL FEATURES

- ✓ Many infections remain asymptomatic despite circulating microfilariae.
- ✓ Initially acute lymphangitis, with fever, painful lymph nodes, edema, and inflammation spreading peripherally from involved lymph nodes (in contrast to bacterial lymphangitis, which spreads centrally) → retrograde lymphangitis → lymphedema with disfigurement of the lower extremities (Elephantiasis).
- ✓ In men, progressing from painful epididymitis to hydroceles that are usually painless but can become very large, with inguinal lymphadenopathy, thickening of the spermatic cord, scrotal lymphedema, thickening and fissuring of the scrotal skin, and occasionally chyluria

DIAGNOSTIC WORKUP

- ✓ Blood smear obtained at night (and staining with Giemsa or hematoxylin and eosin): detection of microfilariae
- ✓ Serological test: elevated levels of antifilarial IgG4

Rx**TREATMENT OF LYMPHATIC FILARIASIS**

- ✓ Patient with lymphedema: Elevation of the affected extremity, exercise, and wearing therapeutic shoes.
- ✓ Diethylcarbamazine (DEC) at dose 2mg/kg per orally x TDS for 10–14 days. Accompanied by allergic symptoms.
- ✓ OR Combination triple therapy with a single per oral dose of Tab. Albendazole 200mg (Zentel) 2 tab (400 mg) PLUS Diethylcarbamazine (DEC) at dose 2mg/kg PLUS Tab. Ivermectin 6mg (Ivermectin) at dose 200 mcg/kg x every year for 3 years is safe and is recommended by WHO in areas not endemic with onchocerciasis or Loa-loa.
- ✓ Co-endemic with Loa-loa: Cap. Doxycycline 100mg (Doxyn) at dose 100–200 mg/day orally for 4–6 weeks.

LYMPHOGRANULOMA VENEREUM (LGV)

Name: Age: Sex: Date:
 B.P: Pulse: Resp. Rate:
 Temperature:

- ✦ **Etiology:** Caused by *Chlamydia trachomatis* serotypes L1, L2 & L3.
- ✦ **Risk factor:** Infection occurs through contact with mucosal trauma or abrasions in the skin of the genital region from receptive fisting, sex toy use, and group sex, and men who have sex with men (MSM).
- ✦ **Associated conditions:** Co-infection with *Neisseria gonorrhoeae*, pelvic inflammatory disease (PID)

CLINICAL FEATURES

- ✦ **Proctitis Stage:** Rectal infection (most common) proctitis or proctocolitis, seen in case of MSM.
 - » **Mild symptoms:** constipation, mucous streaking of stool
 - » **Severe symptoms:** rectal pain, bleeding, and discharge; tenesmus, and systemic symptoms
- ✦ **Primary Stage:** Often asymptomatic = 50% cases. Small, painless genital and anal ulcers (herpetiform), may be accompanied by mucopurulent discharge, can sometimes lead to self-resolving ulcers within few days.
- ✦ **Secondary Stage:** Develops 2–6 weeks after onset of primary infection. Regional lymphadenopathy (groin, inguinal, or pelvic lymph nodes). Lymphadenitis (tender/painful, enlarged) and may form **BUBOES** (inguinal adenitis). **Groove sign** (of Greenblatt) present. Constitutional symptoms like fever, malaise, headache, and myalgia may also be present.
- ✦ **Tertiary Stage:** Occurs if the infection is left untreated or inadequately treated. Manifestations include, chronic lymphadenopathy, rectal strictures, or fistulas (in cases of rectal involvement), genital elephantiasis (rare)
- ✦ **Oral Ulcer Stage:** oral ulceration, which may be followed by cervical lymphadenopathy.

DIAGNOSTIC WORKUP

- ✦ **Nucleic Acid Amplification Tests (NAATs)**
 - » **Specimen:** Urine and lymph node well as swabs of the urethra, rectum, cervix, & genital ulcers.
- ✦ **Anorectal Gram stain:** rectal swab via anoscopy (in proctitis or proctocolitis) → >10 WBCs/HPF.
- ✦ **STI testing:** Syphilis, HIV, gonorrhea, HCV, HBV

Rx

TREATMENT OF LYMPHOGRANULOMA VENEREUM (LGV)

1. **Preventive treatment:**
 - » Sex partners from the preceding 60 days should be identified and treated with the same regimen OR, if no partners in the past 60 days, the most recent partner
 - » **Instruct the patient to avoid all sexual contact until:** Antibiotic course has been completed, Resolution of symptoms. All sexual partners have completed treatment
 - » Consider bubo drainage.
 - » **Retest after completion of treatment.**
 - » Pregnant women: at 4 weeks
 - » Other patients: at 3 months (up to 12 months, if needed)
2. Consider bubo drainage (needle aspiration or I&D) to prevent formation of ulcers and fistulas formation.
3. **Asymptomatic partners/patients who expose to LGV:** Cap. Doxycycline 100 mg orally twice daily (BD) for 7 days
4. **Symptomatic patient with LGV:** Cap. Doxycycline 100 mg orally twice daily for 21 days
 OR Tab. Azithromycin 500mg at dose 1g orally once weekly for 3 weeks.
 OR Tab. Erythromycin base 500 mg (Erythrocin) x orally four times daily (QID) for 21 days



GENITOURINARY CHLAMYDIA (NON-LYMPHOGRANULOMA VENEREUM)

- Name: _____ Age: _____ Sex: _____ Date: _____
 Temperature: _____ B.P: _____ Pulse: _____ Resp. Rate: _____
- It is one of the most common STIs worldwide and one of the most common causes of pelvic inflammatory disease.
 - Etiology:** Caused by *Chlamydia trachomatis* serotypes D-K
 - Transmission:** Transmitted through genital-to-genital contact or oropharyngeal-to-genital contact.

CLINICAL FEATURES

- Mostly infected patients are asymptomatic.
 - Patients of any gender (male and female) may present with urethritis (can cause dysuria or polyuria) or proctitis.
 - Female patients may also present with salpingitis, cervicitis, or symptoms of pelvic inflammatory disease (PID).
 - Muco-purulent vaginal discharge
 - Abnormal uterine bleeding
 - Postcoital bleeding: Bleeding after sexual intercourse.
 - Dyspareunia: Pain during sexual intercourse.
 - Male patients may also present with epididymitis or prostaticitis.
 - Symptoms of **REACTIVE ARTHRITIS** (Reiters syndrome) may also be present.
- Characteristic triad of symptoms consists of reactive arthritis:** 1. Arthritis, 2. Conjunctivitis, and 3. Urethritis.

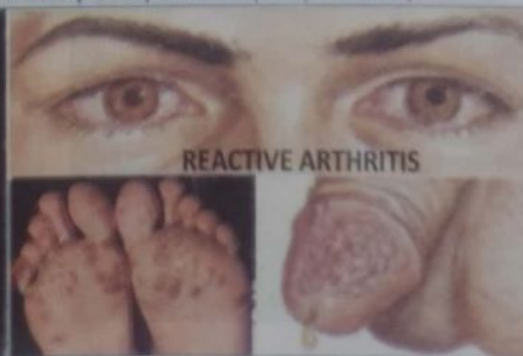
DIAGNOSTIC WORKUP

- Nucleic Acid Amplification Tests (NAATs)**
 - Specimen: swab of an affected site (urethra, endocervix, rectum) OR first-void urine is used.
 - Female patient: vaginal swab (preferred), cervical swab, or first-void urine
 - Male patient: first-void urine (preferred) or urethral swab
 - Suspected exposure with rectal: rectal swab
- ± **Culture:** Can be performed along with NAATs.
 - Specimen: swab of an affected site (urethra, endocervix, rectum) is used
- STI testing:** Syphilis, HIV, gonorrhea, HCV, HBV.



TREATMENT OF NON-LYMPHOGRANULOMA VENEREUM CHLAMYDIA

- Preventive treatment:**
 - Sex partners from the preceding 60 days should be identified and treated with the same regimen OR, if no partners in the past 60 days, the most recent partner
 - Instruct the patient to avoid all sexual contact until:** completion of 7 days antibiotic course or single dose treatment with antibiotics. Resolution of symptoms. All sexual partners have completed treatment
 - Retest after completion of treatment.**
 - Pregnant women: at 4 weeks
 - Other patients: at 3 months (up to 12 months, if needed)
- Assess and treat sexual partners (offer intensive partner therapy if possible) with same regimen for 7 days.
- Initiate antibiotic therapy (even if asymptomatic):** Cap. Doxycycline 100 mg orally twice daily for 7 days OR Cap. Azithromycin 500mg (Azomax) at dose 1g orally once weekly for 3 weeks. (**SAFE IN PREGNANCY**)
Alternative in pregnant women: Cap. Amoxicillin 500 mg (Amoxil) x orally every 8 hours (TDS) for 7 days.



REACTIVE ARTHRITIS

GRANULOMA INGUINALE (DONOVANOSIS)

Name: _____ Age: _____ Sex: _____ Date: _____
 Temperature: _____ B.P: _____ Pulse: _____ Resp. Rate: _____

- Definition: Granuloma inguinale (Donovanosis) is a chronic, relapsing granulomatous anogenital infection due to *Klebsiella granulomatis* (previously known as *Calymmatobacterium granulomatis*).
- Risk factors: Men who have sex with men, Uncircumcised men, Low socioeconomic status
- Transmission: Sexual transmission, Autoinoculation of adjacent skin, Perinatal transmission

Clinical features

- Incubation period: usually 1–12 weeks. Onset: Insidious.
- Painless genital lesion – begin as one or more nodules; eventually ulcerate to form large, forming shallow, sharply demarcated ulcers with a beefy-red lesions that bleed easily. The lesions occur on the skin or mucous membranes of the genitalia or perineal area. **Male:** foreskin, coronal sulcus, glans. **Female:** labia minora, cervix.
- The lesions may spread contiguously from the genital or perineal regions to the lower abdomen and thighs.
- The advancing border maintains a characteristic rolled edge of granulation tissue; the ulcers may become large, purulent, painful, foul-smelling, and difficult to treat. Regional lymph nodes are typically spared.
- Secondary bacterial infections are common as are coinfections with other STIs.
- Can rarely extend to extragenital sites (including the oral cavity, pharynx, and intrabdominal organs)

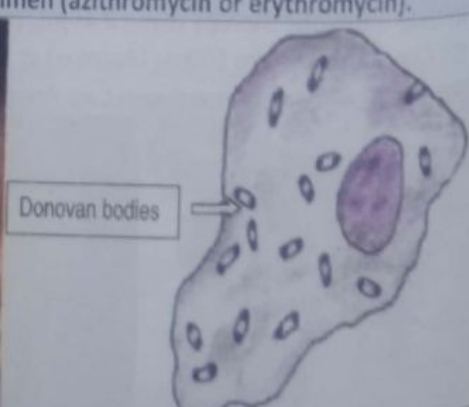
DIAGNOSTIC WORKUP

- Microscopic exam of fluid, tissue scrapings, or biopsy of the genital lesion:
 - Donovan bodies → Pathognomonic cell to diagnose and confirm the disease
 - It is large (25–90 μm).
 - Contains intracytoplasmic cysts filled with bodies that stain deeply with wright stain.
 - Safety-pin shaped bodies within macrophages
- Molecular assays: Can be considered to identify the causative pathogen if Donovan bodies were not detected on microscopy.
- K. granulomatis* is difficult to culture.

Rx

TREATMENT OF GRANULOMA INGUINALE (DONOVANOSIS)

- Tab. Azithromycin 500mg (Azitma, Azomax) at dose 1g (2 tablets) per orally, once weekly or 500 mg daily.
- OR Cap. Doxycycline 100mg (Doxyn, Vibramycin) orally x BD
- OR Tab. Trimethoprim sulfamethoxazole 160/800mg (Septran DS) orally twice daily (BD)
- OR Tab. Erythromycin 500mg (Erythrocin) x QID (4time/day)
- Treatment duration: Duration of therapy is relatively long. The above recommended regimens should be given for 3 weeks or longer and until all lesions have healed.
- Follow-Up: Patients should be followed clinically until signs and symptoms resolve.
- Prevent onward transmission and reinfection: Sex partners from the preceding 60 days should be identified and treated with the same regimen OR, if no partners in the past 60 days, the most recent partner. However, the value of empiric therapy in the absence of clinical signs and symptoms has not been established.
- Pregnant & lactating women should be treated with a macrolide regimen (azithromycin or erythromycin).



CHANCROID

Name:	Age:	Sex:	Date:
Temperature:	B.P:	Pulse:	Resp. Rate:
Definition: Chancroid (also known as soft chancre) is a highly contagious sexually transmitted infection (STI).			
Etiology: <i>Haemophilus ducreyi</i> (short gram-negative bacillus)			
Transmission: sexually transmitted infection			

Clinical features

- Incubation period: 4–10 days
- Very painful genital ulcers:
 - At the site of inoculation, a vesicopustule develops that breaks down to form a painful, soft ulcer, well-demarcated lesion with a grayish necrotic base, surrounding erythema, and undermined edges.
 - There may be multiple lesions due to autoinoculation
 - In male: glans penis, penis shaft, and scrotum
 - In female: vulva and perineal area
- Painful lymphadenitis (Painful inguinal lymphadenopathy) is usually unilateral and consists of tender, matted nodes of moderate size with overlying erythema. These may become fluctuant and rupture spontaneously.
- Additionally with lymph node involvement, fever, chills, and malaise may develop.
- Balanitis (inflammation - head of the penis) & phimosis (tight foreskin) are frequent complications in penile infections.
- Women with cervical infections may have no external signs of infection

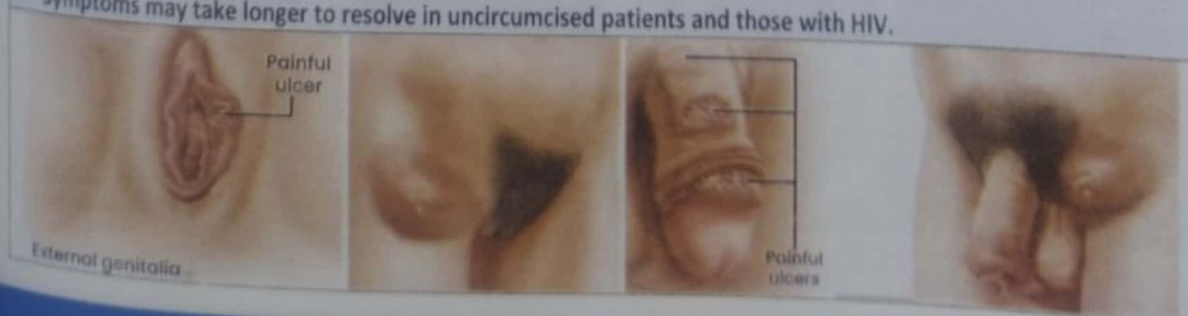
Diagnostic workup

- Diagnostic criteria for chancroid: A probable diagnosis of chancroid can be made if all the following criteria are met.
 1. Presence of painful deep genital ulcers
 2. Tender lymphadenopathy
 3. Negative tests for syphilis (*T. pallidum*)
 4. Negative tests for genital herpes (HSV1 and HSV2)
- Confirmatory investigation: Performed rarely.
 - Gram-stain: gram-negative rods in ulcer exudate (swab sample) suggestive of *Haemophilus ducreyi* infection
 - Culture: Consider in areas where chancroid is highly prevalent.
 - NAAT/PCR



TREATMENT OF CHANCROID

- Tab. Azithromycin 500mg (Azomax) at dose 1g (2 tablets), orally once
- OR Inj. Ceftriaxone 250mg (Oxidil, Titan, Rocephin) x IM, single dose
- OR Tab. Ciprofloxacin 500mg (Ciproxin) x 2 times/day for 3 days.
- OR Tab. Erythromycin 500mg (Erythrocin) TDS for 7 days.
- Follow-up: Patients should be reexamined 3–7 days after therapy initiation. If treatment is successful, ulcers usually improve symptomatically within 3 days and objectively within 7 days after therapy. If no clinical improvement is evident, the clinician should identify another STI and treat it.
- Management of sex partners to prevent onward transmission and reinfection: Sex partners from the preceding 60 days should be identified and treated with the same regimen OR, if no partners in the past 60 days, the most recent partner within 10 days prior to symptom onset.
- Symptoms may take longer to resolve in uncircumcised patients and those with HIV.



HERPES GENITALIS (COLD OR FEVER SORE)

- Definition: Genital herpes (genital herpes simplex or cold or Fever Sore) is a chronic, lifelong viral infection.
- Etiology: Most commonly HSV-2, less commonly HSV-1. Incubation period: 4–7 days. Transmission: sexual contact.

Clinical features

- Affected individuals are often asymptomatic or have mild symptoms but may still be at risk of transmission.
- Skin lesions: may be present in both initial & recurrent infection. The lesions usually crust and heal in 1 week.
 - Prodromal symptoms: redness, swelling, tingling, pain, pruritus
 - The lesions consist of small, grouped vesicles on an erythematous base that can occur anywhere but that most often occur on the vermilion border of the lips, the oral cavity, penile shaft, the labia, the perianal skin, and the buttocks
- Primary infection
 - Genital tract: skin lesions in the anogenital area, cervicitis, white, thick, and/or foul-smelling vaginal discharge
 - Urinary tract: dysuria, urethritis
 - Associated symptoms: fever, headaches, myalgias, malaise, tender and swollen B/L inguinal lymphadenopathy
- Recurrent infection
 - Prodromal symptoms (lasting hours to days): pain or tingling in the genitals, legs, buttocks, and/or hips
 - Skin lesions are usually unilateral, less painful, and of shorter duration than in the initial infection.
- Immunosuppressed patients may have unusual variants, including verrucous or nodular herpes lesions at typical sites of involvement. Lesions of herpes simplex must be distinguished from chancroid, syphilis, lymphogranuloma venereum, pyoderma gangrenosum, or trauma.

DIAGNOSTIC WORKUP

- If lesions are present: Make an initial clinical diagnosis to facilitate timely empiric treatment.
- If lesions are absent: Obtain type-specific HSV testing in selected cases.
- Direct fluorescent antibody slide tests offer rapid, sensitive diagnosis.
- Viral culture or PCR may also be helpful.
- Herpes serology is not used in the diagnosis of an acute genital ulcer.
- Specific HSV-2 serology by Western blot assay or ELISA can determine who is HSV-infected and potentially infectious, but routine HSV-2 screening is not recommended by the USPSTF



TREATMENT FOR GENITAL HERPES

- First clinical episode of infection: Tab. Acyclovir 800mg orally 3 times/day or 400mg orally 5 times/day OR Tab. Famciclovir 250mg orally 3 times/day OR Tab. Valacyclovir 1000mg orally 2 times/day for 7–10 days
- Recurrent episode: Tab. Acyclovir 400–800mg x BD for 5 days (OR 800mg x TDS for 2 days) OR Tab. Famciclovir 500mg once, followed by 250mg 2 times/day for 2 days OR Tab. Valacyclovir 500mg orally 2 times/day for 3 days
- Patients with HIV:
 - Suppressive therapy: Tab. Acyclovir 400–800mg orally 2–3 times/day OR Tab. Famciclovir 500mg orally 2 times/day OR Tab. Valacyclovir 500 mg orally 2 times/day 7–10 days
 - Episodic infections: Tab. Acyclovir 400 mg orally 3 times/day OR Tab. Famciclovir 500mg orally 2 times/day OR Tab. Valacyclovir 1000mg orally 2 times/day for 5–10 days
- Management of sexual partners: Counsel on safer sex practices and STI prevention.
 - Symptomatic: Provide diagnostics and treatment for genital herpes.
 - Asymptomatic: Offer type-specific HSV testing.



UROGENITAL GONOCOCCAL (GONORRHEA) INFECTIONS

- Definition: Gonorrhea infection is a common STI caused by *Neisseria gonorrhoeae* (gonococcus)
- Transmission: Sexual (oral, genital, or anal), Perinatal
- Risk factors: multiple sex partners in recent months, known partner with gonorrhea, prior STI, men who have sex with men (MSM), lack of barrier protection (sex without condom), Asplenia, and complement deficiencies

CLINICAL FEATURES

UNCOMPLICATED GONOCOCCAL INFECTIONS

1. **Gonococcal urethritis:** Mucopurulent urethral discharge (yellow-green or white, possibly blood-tinged), painful urination (dysuria), increase urinary frequency.
 - » In female: genitalia are often asymptomatic; can be associated with: Bartholin gland abscess (pain, edema, and discharge on the labia) and/or vulvovaginitis (rare)
 - » In male: Genitalia may have penile shaft edema/foreskin inflammation and/or prostatitis.
2. **Gonococcal cervicitis:** May be asymptomatic, Mucopurulent, yellow, malodorous cervical/vaginal discharge
 - » On pelvic examination: cervical erythema, cervical pain and bleeding (friable cervix)
 - » Postcoital bleeding (bleeding after sexual activity) or abnormal bleeding between periods.

COMPLICATED GONOCOCCAL INFECTIONS

1. **Gonococcal pelvic inflammatory disease (PID) – For more detail see GYNAE/OBS**
 - » Fever, abdominal pain, pelvic pain and/or dyspareunia
 - » Abnormal intermenstrual bleeding or menorrhagia
 - » Abnormal vaginal discharge (yellow/green color)
 - » May progress to Fitz-Hugh-Curtis syndrome (RUQ pain due to perihepatitis)
2. **Epididymitis** (typically one-sided scrotal pain and swelling) &/or **orchitis** (enlarged, swollen, tender testicles)

DIAGNOSTIC WORKUP

- **Nucleic Acid Amplification Tests (NAATs)**
 - » Specimen: swab of an affected site (urethra, endocervix, rectum) OR first-void urine is used.
 - » For urogenital infections: First-void urine is better in patients with male genitalia, and a vaginal swab is preferred in patients with female genitalia.
- **± Culture:** Can be performed along with NAATs.
 - » Specimen: swab of an affected site (urethra, endocervix, rectum) is used.
 - » Positive chocolate agar culture
- **Gram stain:** Useful in asymptomatic urethritis.
 - » Swab of urethral discharge or secretions
- **STI testing:** Syphilis, HIV, HCV, HBV, Chlamydia

TREATMENT OF UNCOMPLICATED GENITAL GONOCOCCAL INFECTION



- **Preventive treatment:**
 - » Sex partners from the preceding 60 days should be identified and treated with the same regimen.
 - » Instruct the patient to avoid all sexual contact until: 7 days after treatment of the patient and their sexual partners and/or symptoms have resolved.
 - » All patients: Retest at 3 months.
- **Firstline:** Inj. Ceftriaxone 500mg x IM, as a single dose; if body weight > 150 kg then 1g x IM, as a single dose
± Cap. Doxycycline 100mg (Doxyn) x BD for 7 days.
- **Second line:** Inj. Gentamicin 240 mg x IM, as a single dose
AND Cap. Azithromycin 500mg (Azomax) x 2g x once.



TREATMENT OF EPIDIDYMITIS &/OR ORCHITIS

- Preventive treatment as above
- Inj. Ceftriaxone 500mg x IM, as a single dose; if body weight > 150 kg then 1g x IM, once.
+ Cap. Doxycycline 100mg (Doxyn) x BD x 10 days
OR Tab. Levofloxacin 500mg (Leflox) x OD, 10 days



TREATMENT OF PID See GYNEA/OBS FOR MORE DETAIL

- Preventive treatment as above
- **Firstline:** Inj. Ceftriaxone 500mg x IM, as a single dose; if body weight > 150 kg then 1g x IM, as a single dose
+ Cap. Doxycycline 100mg (Doxyn) x BD for 14 days
+ Tab. Metronidazole 400mg (Flagyl) x TDS for 14 days



SYPHILIS

Name: Age: Sex: Date:
Temperature: B.P: Pulse: Resp. Rate:

Clinical manifestation

Primary syphilis

- » Painless LN + painless indurated genital ulcer (hard chancre)
- » Most common site of ulcer is genitalia > mouth, nipple.
- » VDRL negative – Antibodies take 2-3 months to develop.

Secondary syphilis:

- » Skin rashes + condyloma lata at mucocutaneous junction
- » Painless inguinal lymphadenopathy
- » Highly infectious
- » All the serological tests are 100% positive

Tertiary/Latent syphilis: No symptoms, diagnosis by serology only.

Quaternary syphilis:

- » CVS: Aortic aneurysm, Aortic regurgitation
- » Neuro-syphilis: Cerebrospinal fluid examination (CSF) evaluation recommended in all patients
 1. Meningovascular: Stroke, neuropathies
 2. General paresis of insane: Dementia, Psychosis
 3. Argyll Robertson pupil
 4. Tabes Dorsalis: Numbness, Muscular weakness

DIAGNOSTIC WORKUP

- » Serological test – VDRL & RPR test become positive 4–6 weeks after infection or 1–3 weeks after the appearance of a primary lesion- maybe used for secondary, tertiary and quaternary syphilis
- » Investigation of choice for Primary early syphilis: Dark field Microscopy (up to 90% sensitivity)
- » Late diseases: TPA → Detection, Alternative T.Pallidum polymerase chain reaction (PCR)

Rx

PRIMARY, SECONDARY, OR EARLY LATENT SYPHILIS (<1 YEAR)

- » Inj. Benzathine penicillin-G 2.4 million units (Benzibiotic) x Intramuscularly (IM) x once only
- » Alternative medication
 - » Cap. Doxycycline 100mg (Vibramycin, Doxyn) 1-0-1 (BD) x for 14 days
 - » ±Tab. Metronidazole 400mg (Klint, Flagyl) x TDS
 - » OR Inj. Ceftriaxone 1g (Oxidil, Rocephin) x IM/IV x daily for 8–10 days

Rx

LATE LATENT OR UNCERTAIN DURATION (OR >1 YEAR)/ TERTIARY WITHOUT NEUROSYPHILIS

- » Inj. Benzathine penicillin-G 2.4 million units (Benzibiotic) x IM x once weekly for 3 weeks
- » Alternative medication/in case penicillin allergy
 - » Cap. Doxycycline 100mg (Vibramycin, Doxyn) 1-0-1 (BD) x for 28 days
 - » ±Tab. Metronidazole 400mg (Klint, Flagyl) x TDS

Rx

SYMPTOMATIC OR ASYMPTOMATIC NEUROSYPHILIS

- » Inj. Aqueous penicillin-G 18–24MU x IV x given every 4 hourly or as continuous infusion for 10 – 14 days
- » Alternative medication
 - » Inj. Procaine penicillin, 2.4 million units x IM daily
 - » PLUS Tab. Probenacid 500mg orally four times daily for 10 – 14 days
 - » OR Inj. Ceftriaxone 2g (Oxidil, Titan) x IM/IV infusion x daily for 10 – 14 days

BACILLARY DYSENTERY (SHIGELLOSIS)

Name:

Age:

Sex:

Date:

Temperature:

B.P:

Pulse:

Resp. Rate:

Clinical features

SYMPTOMS

- » Duration: 2 – 7 days.
- » Fatigue, malaise, anorexia
- » Urgency to defecate (tenesmus)
- » Abdominal cramping/pain
- » Profuse inflammatory diarrhea
- » Bloody and mucoid stools
- » Passage of formed feces that temporarily relieves the pain.
- » Features of hemolytic uremic syndrome (HUS)

PHYSICAL EXAM

- » Fever
- » Increase bowel sounds.
- » Abdominal tenderness
- » Signs of dehydration.

Diagnostic workup

- » CBC: WBCs normal or ↑, ↑ Hct due to volume depletion, leukocytosis.
- » Stool microscopy: leukocytes, RBCs
- » Stool culture and sensitivity: **+ve**
- » BUN and creatinine: suggest AKI.
- » Serum electrolytes if dehydrated.

Monitoring

- » Most patients with shigellosis recover completely. There is no need for continued monitoring once recovery has occurred. However, monitoring may be indicated for patients with complications.
- » Malnutrition is often caused or exacerbated by more severe shigellosis and will need careful follow-up until the patient has recovered. Patients with hemolytic uremic syndrome may have residual chronic renal impairment and hypertension. Reactive arthritis is likely to require rheumatologic follow-up.



TREATMENT OF MILD-MODERATE BACILLARY DYSENTERY

1. **Oral rehydration therapy (ORS):** The WHO recommends low-osmolality ORS formula for diarrhea in all age group patients.
 - ↳ Osmolar ORS (banana or Orange flavoured)
 - ↳ OR Peditral Low OSM ORS (Lemon/limed or Orange flavoured)
 - ↳ OR Hilyte-R (Rice based – ORS)
 2. **Recommended antibiotics therapy shortens duration of dysentery.**
 - ↳ Tab. Ciprofloxacin 500mg (Cipesta, Novidate, Ciproxen) 1 – 0 – 1 (500mg x BD for 3 days) *CMDT-2024 guidelines*
 - ↳ OR Tab. Levofloxacin 500mg (Cravit, Levoxin) x OD for 3 days
 - ↳ OR Cap. Azithromycin 500mg (Zetro, Azomax) 0 – 0 – 1 (OD) for 3-5 days
 - ↳ OR Inj. Ceftriaxone 1-2g (Oxidil, Rocephin) x diluted in 100ml 0.9% N.S x IV x OD, for 3 days. *Alternative:* Cap. Cefixime 400mg x OD for 5 days (Michigan university of medicine)
 - ↳ OR Tab. Trimethoprim 160mg/Sulfamethoxazole 800mg 1 – 1 – 1 (TDS) for 5 days (Septran DS, Nicotrim forte)
 3. **With abdominal cramps/pain**
 - ↳ Tab. Drotaverine 80mg (Nospa forte, Relispa forte)
 - ↳ OR Tab. Mebeverine 135mg (Colofac, Spasler-P) 1 – 0 – 1 (BD)
 4. **With fever (antipyretic/analgesic)**
 - ↳ Tab. Paracetamol (Panadol, Calpol, Febrol) 1 – 1 – 1 (1 x TDS) OR 2 – 2 – 2 (2 x TDS)
- Dose: 500mg-1000mg (1-2 tablets) x TDS/QID, Max. 4g/day



TREATMENT OF SEVERE BACILLARY DYSENTERY

1. Hospitalization
2. Establish IV access/IV line
3. **IV fluid therapy:** Ringer lactate or normal saline x IV, Once rehydrated, maintenance therapy with ORS is recommended.
4. **Recommended antibiotics therapy shortens duration of dysentery.**
 - ↳ Inj. Ciprofloxacin 400mg/100ml (Cipesta, Novidate) x IV x BD
 - ↳ OR Inj. Ceftriaxone 1-2g (Oxidil, Rocephin) x diluted in 100ml 0.9% N.S x IV x OD, for 3 days.
5. **With abdominal cramps/pain:** Inj. Drotaverine 40mg/2ml (Nospa, Relispa), diluted in 100ml 0.9%NS x IV
6. **With nausea & vomiting:** consider ONE of the following anti-emetics:
 - Inj. Metoclopramide 10mg/2ml (Metacloclon) x IV x TDS.
 - OR Inj. Ondansetron 8mg/4ml (Onset, Onseron) x diluted in 50 to 100 ml of 0.9% NS OR D5%W, IV over 15 minutes.
7. **With fever (antipyretic/analgesic):** Inj. Paracetamol 1000mg/100ml (Paracet, Provas) x TDS/SOS. Maximum dose: 4g/day.

COVID-19 (coronavirus disease 2019)

- **Introduction COVID-19:** COVID-19 is an acute infectious respiratory disease caused by infection with the new coronavirus subtype SARS-CoV-2, first detected a cluster of cases of 'viral pneumonia' in Wuhan, P.R. China, in 31 December 2019. COVID-19 usually presents with fever and upper respiratory symptoms, especially dry cough and often dyspnea; asymptomatic courses and certain other symptoms can also occur.

➤ Incidence and prevalence

- » The disease is currently spreading worldwide
- » It is currently spreading worldwide and is considered a pandemic disease.

➤ Transmission: mainly person-to-person

- » **Primarily via respiratory droplets:** can be emitted during sneezing and coughing as well as loud speech
- » **Via aerosols:** infectious concentrations of viral particles were detected in aerosols for a duration of 3 hours and could last even longer
- » **Direct contact transmission:** especially hand-to-face contact
- » **Fomite (surface) transmission:** viral particles remain infectious on surfaces outside a host for up to a few days depending on the material
 - Latex, aluminum, copper: 8 hours
 - Cardboard: 24 hours
 - Countertops, plastic, stainless steel: 1–3 days
 - Wood, glass: 5 days
- » **Fecal-oral transmission:** Evidence that both SARS-CoV and MERS-CoV are excreted fecally suggests that fecal-oral transmission is possible

- **Zoonotic Disease:** especially from civet cats, camels Bats
- **Incubation period:** 2–14 days (average 5 days)
- **Range from:** Common cold to middle east respiratory syndrome
- **Clinical features range from:** Clinical courses range from: very mild to developing into severe with pneumonia and even critical with life-threatening complications such as ARDS, shock, and organ dysfunction.

➤ Duration of infectiousness:

- » **It is estimated that infected individuals:**
 - Become infectious 2.5 days before the onset of symptoms
 - Cease to be infectious 8 days after the onset of symptoms.
- » The period of greatest infectiousness is at the beginning of symptoms.
- » Viral RNA has been found in respiratory samples long after initial infection, but the presence of detectable viral RNA does not mean that the individual is still infectious.

➤ Immunity and reinfection:

- » There is evidence of immune responses to SARS-CoV-2 following an initial infection or exposure to viral components.
- » But the duration of immunity and its efficacy on the prevention of reinfection is still uncertain.
- » Some studies suggest that the magnitude of the immune response might be dependent on the severity of the disease.
- » Cases of possible reinfection have been reported
- ❖ The transmission of SARS-CoV-2 by asymptomatic individuals can occur, but individuals are most contagious when they are symptomatic.

Clinical features of COVID-19

- **Most common symptoms:** Fever, Fatigue and Dry cough
- **Other symptoms that are less common and may affect some patients include:** Loss of taste or smell, Nasal congestion, Conjunctivitis (also known as red eyes), Sore throat, Headache, Muscle or joint pain, Different types of skin rash, Nausea or vomiting, Diarrhea, Sputum production, Chills or dizziness.

- **Symptoms of severe COVID-19 disease include:** Shortness of breath (an early indicator of rapid deterioration developing), Loss of appetite, Loss of smell (sometimes the only symptom!) and/or taste, Confusion, Persistent pain or pressure in the chest, High temperature (above 38 °C).
- **Other less common symptoms of severe COVID-19 are:** Irritability, Confusion, Reduced consciousness (sometimes associated with seizures), Anxiety, Depression, Sleep disorders, pulmonary embolisms (might be the cause of death in many fatal COVID-19 cases), More severe and rare neurological complications (strokes, brain inflammation, delirium and nerve damage).
- **Course:** The disease has a wide spectrum of severity, ranging from mild to critical. It typically starts with mild symptoms that can progress to more severe courses after about 5–7 days.
 - **Mild (80%)**
 - Uncomplicated course without dyspnea
 - Lasts 1–2 weeks
 - **Severe (15%)**
 - Develops 5–7 days after symptom onset
 - Indicates the disease has progressed to pneumonia
 - Signs include dyspnea and hypoxia
 - Lasts 3–6 weeks
 - **Critical disease (5%)**
 - Signs of severe pneumonia (respiratory failure), acute respiratory distress syndrome (ARDS), coagulopathy, shock, and possibly multiple organ dysfunction syndrome (MODS).
 - Lasts 3–6 weeks
- People of all ages who experience fever and/or cough associated with difficulty breathing or shortness of breath, chest pain or pressure, or loss of speech or movement should seek medical care immediately.

DIAGNOSTIC WORKUP & SCREENING

- **Quantitative reverse transcription PCR (RT-PCR):** Confirms active infection with SARS-CoV-2 from patient specimens. Detect the virus's RNA in a respiratory tract sample.
 - **Method:** detection of viral genome regions specific to SARS-CoV-2
 - **Specimen:** e.g., nasal or pharyngeal swabs or aspirates, sputum, bronchoalveolar lavage.
 - **Rapid IgM-IgG antibody tests:** These tests detect antibodies produced by the body's immune system in response to SARS-CoV-2. COVID-19 serology tests can tell whether or not you have had the viral infection in the past. However, antibody tests are not the preferred tests to diagnose current infections. Antibodies don't show up for about 1–2 weeks after you 1st become sick so antibody tests could miss some early infection
 - **Method:** point-of-care detection of antibodies against SARS-CoV-2 (IgM and IgG antibodies)
 - **Specimen:** serum, plasma, or whole blood
 - **ELISA (Enzyme-Linked Immunosorbent Assay)**
 - **Method:** detection of antibodies against SARS-CoV-2 (IgM, IgA, and IgG antibodies)
 - **Specimen:** serum, plasma, or whole blood
 - **Antigen testing**
 - **Method:** direct detection of SARS-CoV-2 antigens (protein fragments)
 - **Specimen:** nasal swabs, saliva (respiratory samples)
- **Detect the viral proteins of SARS-CoV-2 in respiratory samples.**

How is the sample collected for testing?

- **Proper collection of the appropriate samples is essential for accurate COVID-19 test results.**
- **For RT-PCR or Antigen Testing:** The preferred sample is a swab from the back of your nose. This is called a nasopharyngeal swab, or NP swab. It is collected by having you tip your head back and then a swab (like a long Q-tip with a small head) is gently inserted through one of the nostrils until resistance is met (about 2 inches). It is left in place for several seconds, then rotated several times and withdrawn. This is not painful, but it may be uncomfortable, because your eyes to tear and provoke a coughing spell. CDC guidance says that other samples from the respiratory tract may be collected when it is not possible to collect an NP swab. These include a swab from the back of the throat (oropharyngeal swab) or a swab from the front of your nose (nostril). Sometimes a saliva sample may be collected by having the patient spit into a container.
- **For Antibody Testing:** A blood sample is obtained by inserting a needle into a vein in the arm or by pricking a fingertip and collecting a few drops of blood.

➤ Laboratory studies

- » ABGs: to quickly monitor blood gas tension, oxygen saturation, and pH gases
- » Serum urea, creatinine, and electrolytes (UCE)
- » LFTs and Cardiac enzyme
- » CBC: Observe especially for $\downarrow$ WBC*, $\downarrow$ lymphocytes, and $\downarrow$ platelets. Advanced lymphocytopenia** and thrombocytopenia* $< 100,000/\mu\text{L}$ are signs of a severe course.
- » Inflammatory markers: $\uparrow$ CRP, $\uparrow$ CK, $\uparrow$ LDH, and $\downarrow$ Albumin
- » Procalcitonin (PCT) levels can be elevated in patients with severe courses of the disease, particularly if there is bacterial coinfection with pneumonia and/or sepsis
- » $\uparrow$ Ferritin, $\uparrow$ IL-6
- » Coagulation function: PT/INR, aPTT
- » Urine D/R
- » D-dimer: $\uparrow$ (particularly $> 1 \mu\text{g/L}$) at an early stage indicate a poor prognosis
- » Blood culture: Initially 2 pairs
- » If under undergoing propofol therapy: triglycerides every 3 days

➤ Radiology

- » Chest x-ray: usually bilateral, peripheral opacities in multiple lobes
- » CT scan chest:
Findings: generally bilateral, but a minority are unilateral
 - Ground glass opacities that can progress to solid white consolidation in severe infection
 - Inter- and/or intralobular septal thickening
 - Mixed "crazy-paving" pattern = combination of ground-glass opacity with superimposed interlobular septal thickening and/or intralobular septal thickening

INFECTION CONTROL AND PREVENTIVE MEASURES

☞ Hand hygiene

- Hands should be washed with soap and water or disinfected with a virucidal hand disinfectant after contact with potentially virus-contaminated objects and infected persons
- Avoid touching the face: i.e., the eyes, nose, and mouth.

☞ Respiratory hygiene and cough etiquette

- Avoid coughing or sneezing in the direction of others!
- Use tissues and discard these after use, if tissues are unavailable, coughing and sneezing into the crook of the arm can help keep hands free of contamination.
- Maintain 3–6 ft. (at least an arm's length) distance to coughing or sneezing persons.

☞ Avoid exposure

- Avoid crowds of people (public transport, train stations, airports, and mass events).
- Avoid travel to areas of outbreak.
- Follow local health agency recommendations regarding attendance of events and gatherings.

☞ Masks

1. **General considerations:** Respirators and masks should be used resourcefully with special consideration for healthcare facility (HCF) needs. Sufficient supplies are currently at risk due to the high global demand for personal protective equipment (PPE). If not handled correctly (e.g., by bringing infectious material near the airways when touching the mask to adjust it), face coverings and masks might pose an additional risk of infection to the user.
2. **Cloth face coverings** (everyone in public settings): Explicitly recommended in some regions for public settings in which physical distancing of 2 meters (6 feet) cannot be maintained sufficiently (e.g., grocery stores, pharmacies). Might prevent transmission from asymptomatic infected individuals who are unaware of their infectious status. Might help reduce the diffusion of viral particles and the range of contamination when exhaling, speaking, coughing, or sneezing
3. **Surgical masks:** individuals with confirmed or suspected infection or at risk
4. **N95 respirators:** Indicated in health workers and persons taking care of an infected individual in close settings, such as healthcare facilities (HCFs) or home care settings. N95 respirators and protective eyewear are recommended for health care personnel that are potentially exposed to airborne and fluid hazards (e.g., during invasive procedures). If N95 respirator bottlenecks occur, unvalved N95 respirators may be used with a face shield.

☞ **Infection prevention and control in healthcare settings:** Recommendations vary according to the appropriate health department/agency. Some recommendations from the CDC include:

- **Limit how germs enter HCF**
 - Use telemedicine when possible
 - Manage visitor access and movement
 - Cancel elective procedures
 - Screen patients for respiratory symptoms
 - Encourage respiratory hygiene
- **Isolate symptomatic patients with suspected or confirmed COVID-19**
 - Set up suitable triage areas
 - Place in private rooms with bathroom (if possible) with closed doors
 - Prioritize airborne infection isolation rooms (AIIRs) for patients requiring aerosol-generating procedures (AGPs)
- **Protect health care personnel**
 - Emphasize hand hygiene
 - **Limit contact with patients with suspected or confirmed COVID-19:** respect barriers, limit staff providing care
 - Prioritize respirators
 - Avoid AGPs (Aerosol-generating procedures)
 - Follow recommendations for PPE for COVID-19 and optimize supply

ICU MANAGEMENT

➤ Intensive care unit: (follow hospital guidelines)

- ☞ **Admit to ICU and initiate intubation if any of the following are present:** Signs of respiratory failure, Dyspnea with hypoxemia and Tachypnea (RR > 30/min)
- ☞ **Airway management:** Considering health-care workers have an increased risk of developing COVID-19, especially during high-risk procedures such as intubation, aerosol-generating procedures should be avoided whenever possible!
 - ☞ **Endotracheal intubation:** Rapid-sequence induction is preferred, especially as it minimizes the spreading of infectious aerosols.
 - ☞ To avoid aerosolizing the virus, noninvasive ventilation, high-flow oxygen therapy, bronchoscopy, and nebulizer treatment should be avoided unless there is an absolute indication → If NIPPV (Non-invasive positive pressure ventilation) is indicated (e.g., COPD, asthma, DNI status): attempt with a helmet (vs. face mask) interface.
- ☞ **Mechanical breathing**
 - » **Management recommendations regarding ventilated patients with COVID-19:**
 - Ventilation with lower tidal volumes (LTV) as with ARDS: moderate tidal volume (6 mL/kg).
 - Plateau pressure < 30 cm H₂O
 - Permissive hypercapnia (target pH > 7.3)
 - **PEEP and FiO₂ settings:** adjust as needed according to ARDSnet protocol
 - » The effects and indications of mechanical ventilation for patients with COVID-19 are currently subject to discussion.
 - » High mortality rates among ventilated patients have been reported
 - » **Limited ventilator availability:** High volumes of patients with critical conditions due to COVID-19 have raised concerns regarding ventilator shortages in hospitals during the pandemic.

➤ Extracorporeal blood purification therapy

- ☞ Extracorporeal blood purification therapy can be used to filter inflammatory cytokines from the blood of patients with severe courses of COVID-19 Disease
 - » Use is based on the hypothesis that cytokine storms are important in the etiology of severe courses
 - » The treatment is invasive, so it should only be considered for patients with respiratory failure who are in the intensive care unit (ICU).
 - » A special filter, which can be used with standard extracorporeal purification machines (e.g., for hemodialysis), has been granted an Emergency Use Authorization by the FDA (April 10, 2020).



COVID19 Management of hospitalized patients

1. Maintain ABCD&E
2. Administer O₂ therapy via nasal canula: 1-6 L O₂/min if SpO₂ <94%
Careful with patients with COPD: SpO₂ of 90-94% is appropriate
3. Regular monitoring: BP, Pulse, Respiration, SpO₂, Temperature and lab investigations
4. Supportive care: Adequate hydration, nutrition, and rest
5. Fever management: Inj Paracetamol 1g/100ml x IV x TDS/SOS
6. IV fluid: Inj 0.9% N/S & RL 1L x BD/TDS (Fluid-sparing resuscitation and electrolyte balance as needed)
7. Empiric antibiotic therapy: Antibiotics do not work against viruses; they only work on bacterial infections secondary to COVID: Azithromycin, Inj Piperacillin + Tazobactam etc.
8. Anticoagulation: NIH COVID-19 Treatment Guidelines (See) - Hospitalized patients should be treated with prophylactic dose anticoagulation: Enoxaparin sodium (Clexane)/Fondaparinux (Arixtra)
9. Corticosteroids: E.g. Dexamethasone can help reduce the length of time on a ventilator & save lives of patients with severe and critical illness. Corticosteroids believed to reduce the severity of cytokine storm.
10. To date, there is no specific medicine recommended to prevent or treat the new Coronavirus.
11. **PRONE POSITIONING:** prone positioning increased lung recruitment and improved oxygenation, it improves breathing comfort and oxygenation and is extremely beneficial for COVID-19 patients with compromised breathing, prone position keep alveolar units open and makes breathing easier
 - ✎ Patients were asked to alternate every 2 hours between a prone and supine position during the day and sleep in a prone position at night, as tolerated.
 - ✎ A physician provider supervised the first episode of proning. Patients were asked to self-prone, and nursing staff reminded patients.
 - ✎ While prone, the patient is made to lie on his/her belly using pillows. One can also lie on their right side (right lateral), left side (left lateral) or sit at a 60-90 degree angle in the 'fowler position'.
 - ✎ It is suggest that a patient remain prone for a minimum of 30 minutes to a maximum of 2 hours. "This helps improve ventilation to the lungs and hence oxygen levels start improving."
12. **ANTIVIRAL DRUGS FOR COVID-19**
 - ✎ Inj Remdesivir 200mg/vial ((MDSTEV, Riona, Redzi, Boschivir, IVIREM) x IV infusion in 100ml 0.9% NS loading dose than Inj Remdesivir 100mg IV infusion in 100ml 0.9% NS x OD over 45minutes to 1hour (Total 4-9 doses of 100mg x OD)
 - » The NIH COVID-19 Treatment Guidelines 1/1/21 Panel recommends remdesivir for:
 - Hospitalized adults and pediatric patients (aged ≥12 years & weighing ≥ 40 kg) with COVID-19 who: Require oxygen supplementation BUT Do not need oxygen supplementation through a high-flow device, noninvasive ventilation, invasive mechanical ventilation, or ECMO
 - Might be used in combination with dexamethasone in patients who require oxygen supplementation through a high-flow device or noninvasive ventilation.
 - » Adults Dose: 200 mg IV on day 1, followed by 100 mg once daily for 4-9 days
 - » ****Chloroquine or hydroxychloroquine decrease the antiviral activity of remdesivir: should not coadminister**
13. **Tocilizumab (Actemra):**
 - ✎ Treatment with tocilizumab, whether administered intravenously or subcutaneously, might reduce the risk of invasive mechanical ventilation or death in patients with severe COVID-19 pneumonia
 - ✎ Inj Tocilizumab 200mg/10ml, 400mg/20ml (Actemra) x 400mg IV infusion in 100ml 0.9% N/S stat then repeat 400mg after 12hours once.
14. **Tab. Favipiravir 200mg** (Piravir, Revipar, Favuza, Fapirivir)
 - ✎ Dosage: The usual adult dosage for treatment of influenza virus infection is 1600mg of Favipiravir administered orally BD on 1st Day (8 tablets x BD), followed by 800mg (4 tablets) x BD for five days.
15. **Baricitinib:** Selective JAK1 and JAK2 inhibitor, which blocks cytokine signaling/activity
 - ✎ The FDA issued a EUA on November 19, 2020, authorizing its use in combination with remdesivir in the treatment of hospitalized adult and pediatric (aged ≥ 2 years) patients with COVID-19 who require oxygen supplementation, mechanical ventilation, or ECMO.
16. **Chloroquine and less toxic hydroxychloroquine** - Currently (as of October 2020), there is no evidence supporting the use of these drugs in the treatment of patients with COVID-19.

Presenting features

- Most common symptoms: Fever, Fatigue, Dry cough
- Other symptoms that are less common and may affect some patients include: Loss of taste or smell, Nasal congestion, Conjunctivitis (also known as red eyes), Sore throat and Headache, Muscle or joint pain, Different types of skin rash, Nausea or vomiting, Diarrhea, Sputum production



Treatment of mild-moderate COVID19

- Minimize spread of infection:** Stay in a designated "sick room" away from other people, **Home Isolation:** Use a separate bathroom if possible, Do not leave home except to get medical care, If going out is necessary, avoid public places, public transportation, ridesharing, and taxis, Wear a facemask, Follow general protective measures as described above, Avoid sharing personal household items and wash any used items thoroughly, Clean "high-touch" surfaces daily.
- Supportive care and symptomatic treatment:** Increase intake of Oral fluid, fresh juices, vegetables & fruits
 - Fever and body pain:** Tab. Paracetamol 500mg (Panadol, Calpol) x 1-2 tablets 6 hourly
 - Cough suppressant:** (Syp. Hydrillin OR Syp. Seroline OR Syp. Corex-D) x 2teaspoonfull 3times a day
 - Decrease appetite, energy and immunity:**
 - Syp. Tresorix forte OR Syp. Trimetabol x 2 teaspoonful before meal
 - Tab CAC 1000 OR Abocal 1000 x OD in a glass water
 - Tab. Revital multi Or Tab Surbex-z x PO x OD
 - For secondary bacterial infection:** Tab Azithromycin 500mg (Zetro, Azomax) x OD x 7 – 10 days
 - Tab Prednisolone 5mg (Deltacortril) 40 mg/day PO given in 1-2 divided doses for 7 – 10 days may be given according to patient comorbidities
- Monitor symptoms carefully:** Individuals should seek medical care immediately if symptoms worsen or any emergency warning signs develop, including: NOT MAINTAINING O2 SITUATION, Difficulty breathing/SOB, Persistent pain or pressure in the chest, Change in mental status (e.g., confused, nonresponsive), Signs of cyanosis (e.g., bluish lips)



SEVERE COVID19 ICU



Treatment of SEVERE COVID19 ICU/HDU

- Maintain ABCD&E
- Check SpO2 if <94, Give O2 therapy via nasal canula: 1-6 L O2/min
- Maintain intravenous line (IV cannula)
- Vitals monitoring:** Check BP, PR, RR, Temperature, SpO2
- Send labs: CBC, BUN, creatinine, electrolytes, LFTs, PT, INR, LDH, CRP, RBS, Troponin, Procalcitonin, D-dimer
- IV Fluid: R/L OR 0.9% N/S x 1L x IV x STAT (than as per local guidelines)
- Corticosteroids:** Inj Dexamethasone 4mg/1ml (Decadron) 4-8mg x IV x OD/BD for 7-10 days OR Inj Methylprednisolone (Solu-Medrol) 32mg/day (0.5-1 mg/kg/day) x IV given in 1-2 divided doses for 7-10 days OR Inj. Hydrocortisone 100mg (Solu-cortif) 50 mg IV every 8 hr. for 7 – 10 days
- Inj Piperacillin + Tazobactam 4.5g (Tanzo) x IV infusion in 100ml of 0.9% N/S over 30-40 minutes x TDS
- Inj Tocilizumab 200mg/10ml, 400mg/20ml (Actemra) x 400mg IV infusion in 100ml 0.9% N/S stat then repeat 400mg after 12hours once.
- Inj Remdesvir 200mg (MDSTEV, Riona, Redzi) x IV infusion in 100ml 0.9% NS loading dose than Inj Remdesvir 100mg IV infusion in 100ml 0.9% NS x OD over 45min to 1hour (Total 4-9 doses of 100mg OD)
- Fever:** Paracetamol 1g/100ml infusion x IV x TDS
- Inj Omeprazole 40mg (Risek, Ruling) x IV x OD
- Inj Enoxaparin sodium 40mg, 60mg, 80mg (Clexane) x 100 IU/kg (1.5mg/kg) x SC x OD
- Supportive care:** Adequate hydration, nutrition, and rest
- Admit to ICU and initiate intubation if any of the following are present:** Signs of respiratory failure, Dyspnea with hypoxemia and Tachypnea (RR > 30/min)

FEVER WITH DRY COUGH

DIFFERENTIALS DIAGNOSIS

- » Viral respiratory infections (Flu, COVID19)
- » Bacterial pneumonia
- » Atypical pneumonia
- » Croup, Allergic rhinitis
- » Tonsillitis, Laryngitis, GERD
- » Tuberculosis, Pleural effusion
- » Asthma exacerbation, pulmonary edema
- » Interstitial lung diseases
- » Drug-induced cough (e.g., ACE inhibitors)
- » Acute respiratory distress syndrome (ARDS)

DIAGNOSTIC WORKUP

The investigations should be tailored to the patient's clinical presentation, risk factors, and severity of illness, with the goal of identifying the cause for effective treatment.

- » CBC
- » CRP & ESR
- » Blood culture & sensitivity
- » Chest X-ray (CXR) P.A view
- » Respiratory tests (PFTs, ABG)
- » Serological tests (Mycoplasma, Legionella)
- » Specialized tests based on clinical suspicion.



CONSERVATIVE TREATMENT

1. General care:
 - » Adequate rest, avoiding irritants and hydration.
 - » Honey: Consuming honey or using honey-based cough syrups can help soothe the throat and suppress coughing.
 - » Steam inhalation from a humidifier or a bowl of hot water can help moisten the airways and ease coughing.
2. Antibiotics
 - » Tab. Co-Amoxiclav 625mg OR 1g (Augmentin, Calamox) 1-1-1 (625mg = TDS), OR 1-0-1 (1g = BD)
 - » OR Tab. Azithromycin 500mg (Azitma Azomax, Zetro)
 - » OR Tab. Levofloxacin 500mg (Leflox, Levoxin) 0-0-1 (OD)
3. Cough suppressants for symptomatic relief:
 - » Symp. Hydrillin DM x 2 Teaspoonful (10ml) x TDS
 - » OR Symp. Corex-D x 2 Teaspoonful (10ml) x TDS
 - » OR Symp. Ivy leaf x (Coferb) x 2 Teaspoonful (10ml) x TDS
4. Tab. Loratidine 10mg (Softin, Lorin NSA, Loril) x OD
OR Tab. Cetirizine 10mg (Rigix, Zyretic) x OD
5. For fever: Tab. Paracetamol (Panadol, Calpol, Febrol) 1-1-1 (1 x TDS) OR 2-2-2 (2 x TDS)
Dose: 500mg-1000mg (1-2 tablets) x TDS/QID, Max. 4g/day



FEVER WITH PRODUCTIVE COUGH

DIFFERENTIALS DIAGNOSIS

- » Pneumonia (viral, bacterial, fungal)
- » Sinusitis, Pertussis (Whooping cough)
- » Bronchitis, Acute bronchiolitis
- » Cystic Fibrosis, Bronchiectasis.
- » Tuberculosis
- » Lung cancer.
- » COPD exacerbation
- » Asthma exacerbation
- » Congestive heart failure (CHF)

DIAGNOSTIC WORKUP

The investigations should be tailored to the patient's clinical presentation, risk factors, and severity of illness, with the goal of identifying the cause for effective treatment.

- » CBC, CRP & ESR
- » Sputum culture, gram stain, AFB smear
- » Blood culture and sensitivity
- » Chest X-ray (CXR) P.A view
- » Respiratory tests (PFTs, ABG)
- » Serological tests (Mycoplasma, Legionella)
- » Specialized tests based on clinical suspicion.



CONSERVATIVE TREATMENT

1. General cares are same as FEVER WITH DRY COUGH
2. Antibiotics:
 - » Tab. Co-Amoxiclav 625mg, 1g (Augmentin, Calamox) 1-1-1 (625mg = TDS), OR 1-0-1 (1g = BD)
 - » OR Tab. Clarithromycin XL 500mg (Claritek XL, Klaricid XL)
 - » OR Tab. Azithromycin 500mg (Azitma, Azomax, Zetro)
 - » OR Tab. Levofloxacin 500mg (Leflox, Levoxin)
 - » OR Cap. Cefixime 400mg (Cefim, Cefspan) 0-0-1 (OD)
3. Cough suppressants for symptomatic relief:
 - » Symp. Hydrillin DM x 2 Teaspoonful (10ml) x TDS
 - » OR Symp. Corex-D x 2 Teaspoonful (10ml) x TDS
4. Tab. Loratidine 10mg (Softin, Lorin NSA, Loril) x OD
OR Tab. Fexofenadine 120mg (Fexet, Telfast, Fexo) x OD
Caution is advised when using fexofenadine with azithromycin due to an increased risk of QT prolongation.
5. Tab. Paracetamol (Panadol, Calpol, Febrol) 1-1-1 (1 x TDS) OR 2-2-2 (2 x TDS)
Dose: 500mg-1000mg (1-2 tablets) x TDS/QID, Max. 4g/day

COMMUNITY-ACQUIRED PNEUMONIA (CAP) OUTPATIENT (OPD)

Definition: Community acquired pneumonia is typically characterized by a new lung infiltrate on chest x-ray, together with one or more of the following: fever, chills, cough, sputum production, dyspnea, myalgia, arthralgia, pleuritic pain.

CLINICAL FEATURES

Typical pneumonia

- » Sudden onset of symptoms caused by lobar infiltration.
- » High grade fever & chills.
- » Severe malaise
- » Productive cough with purulent sputum (yellow-greenish)
- » Crackles and bronchial breath sounds on auscultation
- » Decreased breath sounds
- » Enhanced bronchophony, egophony, and tactile fremitus
- » Dullness on percussion
- » Tachypnea and dyspnea (nasal flaring, thoracic retractions)
- » Pleuritic chest pain when breathing, often accompanying pleural effusion.
- » Pain that radiates to the abdomen and epigastric region (particularly in children).

Atypical pneumonia:

- » Slow onset (Indolent course)
- » Dry, non-productive cough
- » Dyspnea/Shortness of breath (SOB)
- » Auscultation often unremarkable
- » Extrapulmonary features are common include fatigue, headaches, sore throat, myalgias, and malaise.

DIAGNOSIS

- » Pneumonia is a **clinical diagnosis** based on clinical history, Physical examination, specific laboratory, and chest x-ray (CXR) findings.
- » Consider microbiological studies and advanced diagnostics based on patient history, comorbidities, severity, and entity of pneumonia.

CRITERIA FOR HOSPITALIZATION

- » Every patient should be assessed individually, and clinical judgment is the most important factor.
- » The pneumonia severity index (PSI) and the CURB-65 score are tools that help to determine whether to admit a patient.

CURB-65 SCORE

- » Confusion (disorientation, impaired consciousness)
- » Serum Urea > 7 mmol/L (20 mg/dL)
- » Respiratory rate $\geq 30/\text{min}$
- » Blood pressure: systolic BP ≤ 90 mmHg or diastolic BP ≤ 60 mmHg
- » Age ≥ 65 years

Interpretation: Each finding is assigned 1 point.

- » CURB-65 score 0 or 1: Patient treated on outpatient (OPD) basis.
- » CURB-65 score ≥ 2 : recommended for short hospitalization.
- » CURB-65 score ≥ 3 (3-5): Consider ICU admission.

Pneumonia severity index (PSI/PORT score) – see google not included

- » Patients are assigned to one of five risk classes based on a more complex point system than in CURB-6.
- » Points are distributed based on patient age, comorbidities, and lab results.

CRITERIA FOR ICU ADMISSION

- » The decision of whether to admit a patient to the intensive care unit (ICU) should be based on clinical judgment.
- » The IDSA/ATS criteria for severe CAP can be used to help triage patients to CAP and guide empiric antibiotic treatment decisions.

IDSA/ATS criteria for severe CAP

*The Infectious Disease Society of America (IDSA) & the American Thoracic Society (ATS)

- | | |
|-----------------------|--|
| Major criteria | <ul style="list-style-type: none"> » Septic shock/need for vasopressors » Mechanical ventilation |
| Minor criteria | <ul style="list-style-type: none"> » Confusion » Body temperature $< 36^\circ\text{C}$ » Hypotension requiring fluid resuscitation. » Respiratory rate $\geq 30/\text{min}$ » $\text{PaO}_2/\text{FiO}_2 \leq 250$ » Leukopenia ($\text{WBC} < 4,000/\text{mm}^3$) » Thrombocytopenia (platelet count $< 100,000/\text{mm}^3$) » $\text{BUN} \geq 20$ mg/dL » Multilobar infiltrates |

Interpretation – Severe CAP: one major criterion or ≥ 3 minor criteria

DIAGNOSTIC WORKUP

Chest x-ray (PA & lateral view) – all suspected patients of pneumonia

- » Findings: new infiltrate provides definitive diagnosis of pneumonia
 - » **Lobar pneumonia**
 - » Opacity of one or more pulmonary lobes
 - » **Presence of air bronchograms:** appearance of translucent bronchi inside opaque areas of alveolar consolidation
 - » **Bronchopneumonia**
 - » Poorly defined patchy infiltrates scattered throughout the lungs.
 - » Presence of air bronchograms
 - » **Atypical or interstitial pneumonia:** Diffuse reticular opacity, Absent (or minimal) consolidation
 - » **Parapneumonic effusion**

Laboratory tests:

- » CBC: Leukocytosis
- » Inflammatory markers: $\uparrow$ CRP, $\uparrow$ PCT
- » Serum procalcitonin (PCT): $\uparrow$ (PCT is an acute phase reactant that can help to diagnose bacterial lower RTIs)
- » ABGs: $\downarrow$ PaO_2
- » LFTs: Usually normal
- » Serum Electrolytes, BUN & creatinine: usually normal, maybe raised in AKI
- » Blood culture in hospitalized setup
- » Sputum culture and gram staining

CT Chest (without IV contrast)

- Advantages: more reliable evaluation of circumscribed opacities, pleural empyema, or sites of consolidation

Indications

- Inconclusive chest x-ray
- Recurrent pneumonia
- Poor response to treatment

ANTIBIOTIC TREATMENT FOR CAP**Low severity CAP (CURB-65 score 0–1)**

- Cap. Amoxicillin 500 mg x TDS
- If patient is allergic to penicillin:
 - Cap. Doxycycline 200mg x BD
 - OR Tab. Azithromycin 500mg OR
 - Tab. Clarithromycin 500mg x BD

Moderate severity CAP (CURB-65 score 2)

- Cap. Amoxicillin 500mg-1g x TDS (or IV if oral medication not possible, treat as inpatient 'below')
- If patient is allergic to penicillin
 - Tab. Levofloxacin 500mg x OD
 - OR Tab. Moxifloxacin 400mg x OD

Severe CAP (CURB-65 score 3–5)

- Treat as inpatient/ICU management

- Duration of treatment: 5 to 7 days of therapy is usually sufficient.

**COMMUNITY-ACQUIRED PNEUMONIA (CAP)****Previously healthy patients without comorbidities or risk factors for resistant pathogens**

- Cap. Amoxicillin 500mg to 1g (Amoxil, Zeemox) x TDS
- OR Cap. Doxycycline 100mg (Vibramycin, Doxyn) x Twice daily
- OR Tab. Azithromycin 500mg (Azomax) x 500mg on day-1, followed by 250mg once daily for 4 days or 500mg OD for 3 days.
- OR Tab. Clarithromycin 500mg (Claritek, Klaricid) x Twice daily.

Patients with comorbidities or risk factors for resistant pathogens

- Single therapy (Monotherapy):** with a Resp. fluoroquinolone
 - Tab. Levofloxacin 750mg (Leflox) x Once daily
 - OR Tab. Moxifloxacin 400mg (Avelox, Moxiget) x Once daily
 - OR Tab. Gemifloxacin 320mg (Grat, Gemi) x Once daily

Combination therapy

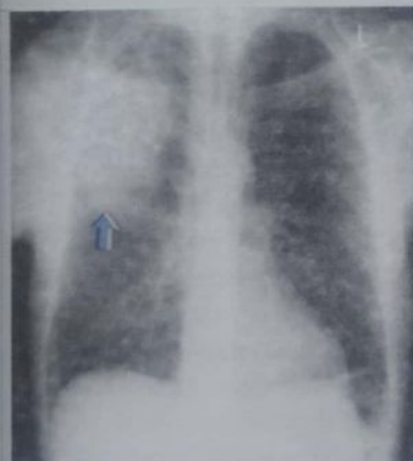
- Tab. Amoxicillin/clavulanic acid 1g (Augmentin) x BD
- OR Cap. Cefuroxime 250mg (Zinacef, Zecef) x 500mg x BD
- OR Tab. Cefpodoxime 200mg (Prelox, Orelox) x BD

PLUS, one of the following:

- OR Cap. Doxycycline 100mg (Vibramycin) x two time daily
- OR Tab. Azithromycin 500mg (Azomax) x 500mg on day-1, followed by 250mg OD for 4 days or 500mg OD for 3 days.
- OR Tab. Clarithromycin 500mg (Claritek, Klaricid) x BD

Supportive treatment

- Supportive care: Adequate hydration, nutrition, and rest
- Anti-tussive: Syp. Corex-D or Syp. Hydrillin x 2 TSP x TDS
- Fever: Tab. Paracetamol 500mg (Panadol) x 1-2 tablets x TDS
- Calcium/vitamins supplement: Abocal or CAC-1000 x OD
- Antihistamine: Tab. Loratadine 10mg x OD

**Right lung opacity**

- X-ray chest (PA view):** Posterior-anterior chest radiograph showing right upper lobe consolidation in a patient with community-acquired pneumonia.

Source: © Durrington HJ, et al./BMJ

**Right upper lobe pneumonia**

- Chest x-ray (PA view):** There is heterogeneous right upper lobe consolidation with air bronchograms.

Source: © IMPP

**Left upper lobe pneumonia**

- Chest x-ray (PA view):** A large, homogeneous opacification (green overlay) can be seen over the left upper lobe. It is also obscuring the left heart border and left pulmonary vessels. This appearance is typical of airspace consolidation due to left upper lobe pneumonia.

COMMUNITY-ACQUIRED PNEUMONIA (CAP) INPATIENT (WARD)



1. Stabilize patients using ABCD&E approach.
2. Establish large-bore intravenous (IV) access.
3. Vitals monitoring: Check BP, PR, RR, Temperature
4. Check SpO₂ if <94 administer O₂ therapy via nasal canula at 1-6L O₂/minutes
5. Obtained investigations: CBC, BUN, Creatinine, Electrolytes, LFTs, PT & INR, LDH, CRP, ESR, RBS, Cardiac troponin, Procalcitonin D-dimer, blood culture, sputum for culture and gram stain.
6. Hydration with PO fluids or IV fluids with Ringer Lactate OR 0.9% Normal saline
7. **Empiric antibiotic therapy for community-acquired pneumonia (CAP): Duration for 5 – 7 days**
 - ↳ **Combination therapy for Non-ICU/non-severe & ICU/severe patients**
 - Inj. Ampicillin-Sulbactam 1.5g to 3g (Ambac) x IV x QID (every 6 hours)
 - OR Inj. Amoxicillin-Sulbactam 1.5g to 3g (Bactamox) x IV x QID (every 6 hours)
 - OR Inj. Ceftriaxone 2g (Titan, Rocephin) x IV x OD (every 24 hours)
 - OR Inj. Cefotaxime 1 to 2g (Claforan, Cefotax) x IV x TDS/BD (every 8-12 hours)
 - PLUS, ONE of the following:**
 - Inj. Azithromycin 500mg/vial (Azitma) x IV x OD (can also be given per orally in tablet form)
 - OR Inj. Clarithromycin 500mg/vial (Klaricid) x IV x BD (can also be given per orally in tablet form)
 - ↳ **OR Monotherapy (Single antibiotic treatment) for non-ICU/non severe patient**
 - Inj. Levofloxacin 500mg/100ml or 750mg/150ml (Leflox) x IV x OD
 - OR Inj. Moxifloxacin 400mg/250ml (Moxiget, Mofest) x IV x OD
- OR Empiric antibiotic therapy for Risk factors for Pseudomonas aeruginosa**
 - ↳ **Combination therapy:**
 - Inj. Piperacillin + Tazobactam 4.5g (Tanzo, Tazocin EF) x IV x TDS (If severe illness than every 6 hours)
 - OR Inj. Ceftazidime 1g to 2g (Fortum) x IV x (every 8 hours)
 - OR Inj. Cefepime 1g to 2g (Uceph) x IV x TDS (every 8 hours)
 - OR Inj. Meropenem 0.5 to 1g (Meronem, Penro) x IV x TDS (every 8 hours)
 - OR Inj. Imipenem-cilastatin 500mg to 1g (Cilapen, Tienam) x IV x QID (every 6 hours)
 - ↳ **PLUS, ONE of the following:**
 - Inj. Azithromycin 500mg/vial (Azitma) x IV x OD
 - OR Inj. Clarithromycin 500mg/vial (Klaricid) x IV x BD
 - OR Inj. Levofloxacin 500mg/100ml (Leflox, Qumic) x IV x OD
 - OR Inj. Moxifloxacin 400mg/250ml (Moxiget, Mofest) x IV x OD
8. **Corticosteroids:** Corticosteroids are not routinely recommended as adjunct therapy.
If indicated: Inj. Dexamethasone 4mg/1ml (Decadron) at dose 4-6mg x IV x BD for 5-7 days
9. **With fever:** Inj. Paracetamol 1g/100ml (Provas) x IV x TDS/SOS
10. **Gastroprotective:** Inj. Omeprazole 40mg (Risek, Ruling) x IV x OD
11. **Thromboprophylaxis (high risk patient):** Inj Enoxaparin sodium 40mg or 60mg or 80mg (Clexane) x 100 IU/kg (1.5mg/kg) x SC x OD. **Alternative:** Inj Fondaparinux (Arixtra) 5-10mg x SC x OD
12. **Admit to ICU and initiate intubation if any of the following are present:**
 - ↳ Signs of respiratory failure
 - ↳ Dyspnea with hypoxemia
 - ↳ Tachypnea (Respiratory rate > 30/minute)
13. Monitor and record pupillary reflexes, GCS level and urine output.
14. **Supportive care:** Hydration, nutrition & sufficient rest (not absolute bed rest) and physical therapy.
15. Identify and treat underlying cause and electrolyte imbalance.



NOSOCOMIAL PNEUMONIA/HOSPITAL-ACQUIRED PNEUMONIA (HAP)

TREATMENT OF NOSOCOMIAL PNEUMONIA/HAP



1. Stabilize patients using ABCD&E approach.
2. Establish large-bore intravenous (IV) access.
3. Vitals monitoring: Check BP, PR, RR, Temperature
4. Check SpO₂ if <94 administer O₂ therapy via nasal canula at 1-6L O₂/minutes
5. Obtained investigations: CBC, BUN, Creatinine, Electrolytes, LFTs, PT & INR, LDH, CRP, ESR, RBS, Cardiac troponin, Procalcitonin D-dimer, blood culture, sputum for culture and gram stain.
6. Hydration with PO fluids or IV fluids with Ringer Lactate OR 0.9% Normal saline
7. Empiric antibiotic therapy for Hospital-Acquired Pneumonia (HAP): Duration for 7 days

Patients not at high risk for mortality and without risk factors for MRSA infection

Monotherapy (Single antibiotic treatment) with

- Inj. Imipenem-cilastatin 500mg (Cilapen, Tienam) x IV x QID (every 6 hours)
- OR Inj. Cefepime 2g (Uceph) x IV x TDS (every 8 hours)
- OR Inj. Piperacillin + Tazobactam 4.5g (Tanzo, Tazocin EF) x IV x QID (every 6 hours)
- OR Inj. Meropenem 1g (Meronem, Penro) x IV x TDS (every 8 hours)
- OR Inj. Levofloxacin 750mg/150ml (Leflox) x IV x OD

Patients not at high risk for mortality but with risk factors for MRSA infection

Combination therapy with

- Inj. Linezolid 600mg/300ml (Ecacil) x IV x (every 12 hours)
- OR Inj. Vancomycin 500mg or 1g x IV at dose 15mg/kg x TDS or BD, adjusted according to serum vancomycin concentration goal to target trough level = 15-20mg/mL (consider loading dose of 25-30mg/kg once for seriously ill patients. Maximum 2g per dose)

PLUS, One of the following:

- Inj. Piperacillin + Tazobactam 4.5g (Tanzo, Tazocin EF) x IV x TDS (If severe than every 6 hourly)
- OR Inj. Cefepime 2g (Uceph) x IV x TDS (every 8 hours)
- OR Inj. Ceftazidime 2g (Fortum, Fortazim) x IV x TDS (every 8 hours)
- OR Inj. Imipenem-cilastatin 500mg (Cilapen, Tienam) x IV x TDS (every 8 hours)
- OR Inj. Meropenem 0.5g to 1g (Meronem, Penro) x IV x TDS (every 8 hours)

Patients at high risk for mortality & Patients with structural lung disease:

Consider combine therapy with Linezolid or Vancomycin PLUS any two of the following (avoid combining two β -lactams): Piperacillin/Tazobactam, Cefepime, Ceftazidime, Meropenem, Imipenem +cilastatin.

8. Corticosteroids: Corticosteroids are not routinely recommended as adjunct therapy.
If indicated: Inj Dexamethasone 4mg/1ml (Decadron) 4-6mg x IV x BD for 5-7 days
9. With fever: Inj. Paracetamol 1g/100ml (Provas) x IV x TDS
10. Gastroprotective: Inj. Omeprazole 40mg/vial (Risek, Ruling) x IV x OD
11. Thromboprophylaxis (high risk patient): Inj. Enoxaparin sodium 40mg or 60mg or 80mg (Clexane) x 100 IU/kg (1.5mg/kg) x SC x OD. Alternative: Inj. Fondaparinux (Arixtra) 5 – 10mg x SC x OD
12. Admit to ICU and initiate intubation if any of the following are present:
 - Signs of respiratory failure
 - Dyspnea with hypoxemia
 - Tachypnea (Respiratory rate > 30/minute)
13. Monitor and record pupillary reflexes, GCS level and urine output.
14. Supportive care: Hydration, nutrition & sufficient rest (not absolute bed rest) and physical therapy.
15. Identify and treat underlying cause and electrolyte imbalance.



VENTILATOR-ASSOCIATED PNEUMONIA (VAP)



TREATMENT OF VENTILATOR-ASSOCIATED PNEUMONIA (VAP)

1. Stabilize patient using ABCD&E approach.
2. Establish large-bore intravenous (IV) access.
3. Vitals monitoring: Check BP, PR, RR, Temperature
4. Check SpO₂ if <94 administer O₂ therapy via nasal canula at 1-6L O₂/minutes
5. Obtained investigations: CBC, BUN, Creatinine, Electrolytes, LFTs, PT & INR, LDH, CRP, ESR, RBS, Cardiac troponin, Procalcitonin D-dimer, blood culture, sputum for culture and gram stain.
6. Hydration with PO fluids or IV fluids with Ringer Lactate OR 0.9% Normal saline
7. Empiric antibiotic therapy for ventilator-associated pneumonia (VAP) for 7 days is usually sufficient.

Recommended combination therapy**1. An antipneumococcal, antipseudomonal β -lactam**

- Inj. Aztreonam 2g/vial (Azactam) x IV x BD (every 12 hours)
- OR Inj. Imipenem-cilastatin 500mg (Cilapen, Tienam) x IV x QID (every 6 hours)
- OR Inj. Meropenem 0.5 to 1g (Meronem, Penro) x IV x TDS (every 8 hours)
- OR Inj. Ceftazidime 2g (Fortum, Fortazim) x IV x TDS (every 8 hours)
- OR Inj. Cefepime 2g (Uceph) x IV x QID (every 6 hourly)
- OR Inj. Piperacillin + Tazobactam 4.5g (Tanzo, Tazocin EF) x IV x TDS (If severe than 6 hourly)

2. PLUS, ONE of the following antibiotics with MRSA activity:

- Inj. Linezolid 600mg/300ml (Ecacil) x IV x BD (every 12 hours)
- OR Inj. Vancomycin 500mg or 1g (Vancomycin) x IV at dose 15mg/kg x 3 times or twice daily adjusted according to serum vancomycin concentration goal to target trough level = 15-20mg/mL (consider loading dose of 25-30mg/kg once for seriously ill patients. Maximum 2g/dose)

3. PLUS, ONE of the following:

- OR Inj. Imipenem-Cilastatin 500mg (Cilapen, Tienam) x IV x QID (every 6 hours)
- OR Inj. Meropenem 1g (Meronem, Penro) x IV x TDS (every 8 hours)

8. Corticosteroids: Corticosteroids are not routinely recommended as adjunct therapy.

If indicated: Inj. Dexamethasone 4mg/1ml (Decadron) 4-6mg x IV x BD for 5-7 days

9. With fever: Inj. Paracetamol 1g/100ml (Provas) x IV x TDS/SOS**10. Gastroprotective:** Inj. Omeprazole 40mg/vial (Risek, Ruling) x IV x OD**11. Thromboprophylaxis** (high risk patient): Inj. Enoxaparin sodium 40mg or 60mg or 80mg (Clexane) x 100 IU/kg (1.5mg/kg) x SC x OD. **Alternative:** Inj. Fondaparinux (Arixtra) 5-10mg x SC x OD**12. Monitor and record** pupillary reflexes, GCS level and urine output.**13. Supportive care:** Hydration, nutrition & sufficient rest (not absolute bed rest) and physical therapy.**14. Antitussives, Expectorants and mucolytics** (N-Acetylcysteine 200mg sachets (Mucolator) x PO/NG^{tube})**15. Identify and treat** underlying cause and electrolyte imbalance.

CHLAMYDIA PSITTACI PNEUMONIA

Chlamydia Psittaci Pneumonia

Clinical features:

- Present as atypical pneumonia:
 - Slow onset, low grade fever
 - Dry cough, persistent cough
 - Mild dyspnea.
- Extra-Pulmonary Symptoms: Headache, Arthralgia, myalgia, nausea, vomiting, and diarrhea.
- Special features: Hepatitis
- On auscultation: Broncho-Breathing (wheezing) and coarse crepitation.

Diagnostic workup

- Chest X-ray: Bronchopneumonia = diffuse, lobar consolidation/infiltrates with air bronchograms.
- CBC: WBCs – Normal, may be ↑ Neutrophils.
- LFTs: deranged (↑↑↑)
- PCR – High sensitivity & specificity
- Test of choice: serology – Anti-chlamydial antibody, reveals 4-fold rise in IgG or presence of IgM.

Complication:

- Endocarditis
- Myocarditis
- Multi-organ failure

- Agents: Obligate Intracellular, zoonotic disease
- Source: Birds (parrot) faeces/stool
- Mode of transmission: via aerosols of birds faeces
- Incubation period: 1–3 weeks
- Risk factors:
 - Exposure to birds, especially pet birds that are sick
 - Fond of having birds, overcrowding
 - Pet shop employees/owner
 - Occupational exposure to poultry



Treatment of Chlamydia Psittaci Pneumonia

1. Tab. Azithromycin 500mg (Azomax) x OD for 5 days
OR Cap. Doxycycline 100mg (Doxyn) x BD for 2-3 weeks
OR Tab. Levofloxacin 500mg (Leflox) x OD for 7-14 days
OR Tab. Moxifloxacin 400mg (Avelox) x OD for 10 days
2. For fever: Tab. Paracetamol 500mg (Calpol, Panadol)
I – I – I (1 x TDS) OR 2 – 2 – 2 (2 x TDS) Max. 4g/day
Dose: 500mg-1000mg (1-2 tablets) x TDS/QID
3. Cough suppressants for symptomatic relief:
 - Syp. Hydrillin DM x 2 Teaspoonful (10ml) x TDS
 - OR Syp. Corex-D x 2 Teaspoonful (10ml) x TDS
 - OR Syp. Ivy leaf x (Coferb) x 2 TSP (10ml) x TDS



MYCOPLASMA PNEUMONIA

Mycoplasma Pneumonia

Clinical features

- Present as atypical pneumonia:
 - Slow onset, low grade fever
 - Persistent cough, dry cough
 - Mild dyspnea.
- Extra-Pulmonary Symptoms:
 - Headache, arthralgia, myalgia
 - Nausea, vomiting, and diarrhea.
- Extra-Pulmonary involvement:
 - Special features: Autoimmune hemolytic anemia (Cold agglutination type)
- On auscultation: Broncho-Breathing (wheezing) and coarse crepitation.

Diagnostic workup

- Chest X-ray: shows patchy or diffuse interstitial infiltrates (Bronchopneumonia).
- CBC: WBCs – Normal or slightly raised, ↓ Hb.
- Inflammatory markers: ↑ CRP
- LFTs: deranged, BUN & creatinine: ↑
- Marker of hemolysis + positive
- Coomb's test + positive
- PCR: from nasopharyngeal swab
- Investigation of choice: Anti-mycoplasma IgG antibody (Most Specific) – reveals High titer of cold agglutinins (IgM antibodies)

- Agents: wall less bacteria, mycoplasma pneumoniae is the most common cause of atypical pneumonia.
 - Pneumonia → Not responding to penicillin group.
- Mode: Community Acquired Pneumonia (CAP) 2nd leading cause
- Risk factors More common in patients < 30 years of age, living in close contact, college students living in dormitories, military recruits, prisoners, most common in the ambulatory setting.
- Associated conditions: Cold autoimmune hemolytic anemia, erythema multiforme, acute interstitial nephritis, bacterial myocarditis.



TREATMENT OF MYCOPLASMA PNEUMONIA

1. Tab. Azithromycin 500mg (Azomax, Azitma) x OD for 5 days.
OR Tab. Clarithromycin XL 500mg (Claritek XL, Klaricid XL)
0 – 0 – I x 1 tablet OD for 10-14 days
OR Tab. Levofloxacin 500mg (Leflox) x OD for 7-10 days.
OR Tab. Moxifloxacin 400mg (Avelox) x OD for 10 days.
2. For fever: Tab. Paracetamol 500mg (Calpol, Panadol)
I – I – I (1 x TDS) OR 2 – 2 – 2 (2 x TDS)
Dose: 500mg-1000mg (1-2 tablets) x TDS/QID, Max. 4g/day
3. Cough suppressants for symptomatic relief:
 - Syp. Hydrillin DM x 2 Teaspoonful (10ml) x TDS
 - OR Syp. Corex-D x 2 Teaspoonful (10ml) x TDS
 - OR Syp. Ivy leaf x (Coferb) x 2 TSP (10ml) x TDS

LEGIONELLA PNEUMONIA (LEGIONNAIRES DISEASE/LEGIONELLOSIS)

△ Legionella pneumonia

C/C:

- » Present as atypical pneumonia:
 - ↳ Slow onset, low grade fever
 - ↳ Persistent cough, dry cough
 - ↳ Mild dyspnea.
- » Extra-pulmonary symptoms:
 - ↳ Headache, Arthralgia, myalgia
 - ↳ Nausea, vomiting, and diarrhea.
- » Special features:
 - CNS: Fits/Seizures, Confusion, ALOC.
 - Liver: Hepatitis, Hepatic encephalopathy
- » On auscultation: Broncho-Breathing (wheezing) and coarse crepitation

Diagnostic workup

- » Chest X-ray: Bronchopneumonia = diffuse, interstitial infiltrates (Bi-basal infiltrates).
- » CBC: WBCs elevated.
- » LFTs: deranged
- » Legionella urinary antigen test: The most important diagnostic tool (Rapid test, but only detects serogroup-1).
- » Urinalysis: Hematuria, proteinuria
- » Serum electrolytes: ↓ Sodium – Dilutional hyponatremia (Pneumonia+ hyponatremia = legionella)
- » Legionella Pneumobilia PCR: high sensitivity and high specificity from sputum, bronchoalveolar lavage.
- » Serology test: a 4-fold rise in antibody titer, useful for diagnosing past or recent infections.

Note: The antibody test low specificity and sensitivity, and seroconversion can take up to 12 weeks. Therefore, more rapid tests like the urinary antigen tests or PCR (NAAT) are used more often.

- » Agents: Gram-negative non-enteric rod
- » Source: Moist Places
- » Transmission sites: aspiration of contaminated water/soil
 - » Air conditioning**
 - » Hot tubs
 - » Swimming pools
- » Risk factors: More common in the elderly, start of summer season, Traveler's pneumonia (Confined travel accommodations: e.g., cruise ships, hotels, resorts), smoking, workers at water company, immunosuppression, hospitalization.
- » Associated conditions: Legionnaires disease (most common) = confusion + encephalopathy with atypical pneumonia, Pontiac fever (self-limited)

Rx

TREATMENT OF LEGIONELLA PNEUMONIA

1. Tab. Levofloxacin 750mg (Levoxin, Leflox) x OD for 7-14 days
OR Tab. Moxifloxacin 400mg (Avelox) x OD for 7-10 days
OR Cap. Azithromycin 500mg (Azomax) x OD for 7-10 days
± Consider addition of rifampicin: If patients are unresponsive to monotherapy, consider addition of rifampicin.
2. For fever: Tab. Paracetamol 500mg (Calpol, Panadol) 1-1-1 (1 x TDS) OR 2-2-2 (2 x TDS)
Dose: 500mg-1000mg (1-2 tablets) x TDS/QID, Max. 4g/day
3. Cough suppressants for symptomatic relief:
 - ↳ Syp. Hydrillin DM x 2 Teaspoonful (10ml) x TDS
 - ↳ OR Syp. Corex-D x 2 Teaspoonful (10ml) x TDS
 - ↳ OR Syp. Ivy leaf x (Coferb) x 2 TSP (10ml) x TDS

△ Staphylococcal Pneumonia

C/C:

- » Risk factors: I/V drug abuser, post-influenza virus
 - » Features of Typical pneumonia such as sudden onset of high-grade fever with chills and rigors, Productive cough with sputum, Mild to severe dyspnea, malaise, fatigue, and Pleuritic chest pain
 - » On auscultation: Broncho-Breathing and coarse crepitation on auscultation
- #### Diagnostic workup
- » Chest X-ray: Bilateral cavitary Bronchopneumonia
 - » CBC: WBCs ↑↑↑
 - » Investigation of choice: Sputum culture

STAPHYLOCOCCAL PNEUMONIA

- » Agents: Most common cause = Staphylococcus aureus.
- » Source: infected person
- » Mode of Transmission: Droplet infection
- » Mode: 1.CAP, 2.HAP → MRSA
- » Risk factors: I/V drug abuser, post-influenza virus

Rx

See treatment of CAP & HAP as explained above

LUNG ABSCESS

Definition: Lung abscess is a circumscribed collection of pus in the lung that leads to cavity formation.

Clinical classification:

- » **Acute lung abscess:** Symptoms present for <2 weeks, and usually only for a few days.
- » **Subacute lung abscess:** Symptoms present for ≥2 weeks.
- » **Chronic lung abscess:** Symptoms present for >1 month.
- » **Primary lung abscess:** Occurs in the absence of underlying medical conditions. Involve in 80% cases.
- » **Secondary lung abscess:** Associated with comorbidities such as obstructive airway disease, neoplasms, immunosuppression, diabetes mellitus, and extrapulmonary infection or sepsis.

ETIOLOGY

1. **Risk factors:** Poor oral hygiene, Impaired swallowing, Immunosuppression, Alcoholism, ASOC (Seizures, Dementia)
2. **Most commonly due to:** 1. Aspiration of oropharyngeal material, 2. Bronchial obstruction. (e.g. Cancer), 3. Sequela of bacterial pneumonia infection.
3. **Common pathogens:** Bacteroides, Peptostreptococcus, Fusobacterium
4. **Less commonly by:** monomicrobial lung abscess caused by *S. aureus*, *K. pneumoniae*, *Strept. pyogenes* or *anginosus*
5. Commonly seen in the right lung than the left → result of wider and straighter right mainstem bronchus.
6. If multiple foci present the cause is most likely hematogenous spreading

△ Lung abscess

C/C:

Indolent presentation with symptoms that evolve over weeks to months

- » **Constitutional symptoms:** Fever, malaise, anorexia, weight loss
- » Cough with expectoration of foul-smelling purulent sputum suggests anaerobic infection.
- » Night sweats
- » Hemoptysis

DIAGNOSTIC WORKUP

- » **Chest X-ray:** may reveals lobar consolidation with central cavitation, an air-fluid level, and thick and irregular cavity walls.
- » **Upright position:** right lower lobe
- » **Recumbent position:** right upper or middle lobe
- » **CBC:** Raised WBCs, anemia
- » **Sputum gram stain:** +ve
- » **Sputum culture & sensitivity:** +ve
- » **Blood culture:** may be also +ve
- » **Contrast enhanced CT chest:** shows thick-walled, usually round cavity with irregular margins forming an acute angle with chest wall, no signs of compression of surrounding lung.
- » **D-dimer:** rule out embolism.

Duration of antibiotic: For 3 weeks but varies depending on clinical response. Some experts recommend treatment until the abscess cavity has resolved on imaging.



TREATMENT OF LUNG ABSCESS

- » Hospitalize the patient and start immediate empiric antibiotic therapy (after obtaining culture samples of patient).
- » **Supportive treatment:** Fever and pain treatment, oxygenation.
- » **Consider the following consults as appropriate:** Pulmonary, Infectious disease and cardiothoracic surgery or interventional radiology for patients with large abscesses.
- » **Identify and treat the underlying cause.**
- » **Empiric antibiotic therapy for bacterial lung abscess**
 - **Patient WITH NO risk factors for MRSA infection:**

Monotherapy (single agent) with any of the following:

 - » Inj. Imipenem-Cilastatin 500mg (Cilapen, Tienam) x IV x QID
 - » OR Inj. Meropenem 1-2g (Meronem) x IV x TDS
 - » OR Inj. Ertapenem 1g (Invanz, Ernem) x IV x OD
 - » OR Inj. Moxifloxacin 400mg/250ml (Moxiget, Mofest) x OD
 - » OR Inj. Clindamycin 300mg/2ml at dose 600mg x IV x TDS, then 300mg x PO x TDS (be cautious for *C. difficile* infection)

OR Combination therapy:

 - » Inj. Metronidazole 500mg/100ml (Flagyl) x IV x TDS
 - » PLUS, any one of the following:
 - ↳ Inj. Ampicillin-sulbactam 1.5g to 3g (Ambac) x IV x TDS
 - ↳ OR Inj. Piperacillin-tazobactam 4.5g (Tanzo) x IV x TDS
 - ↳ OR Inj. Ceftriaxone 2g (Rocephin, Oxidil) x IV x OD
 - ↳ OR Inj. Levofloxacin 750mg/150ml (Leflox) x IV x OD
 - **Patient with suspected for MRSA infection**

Monotherapy (single agent) with any of the following:

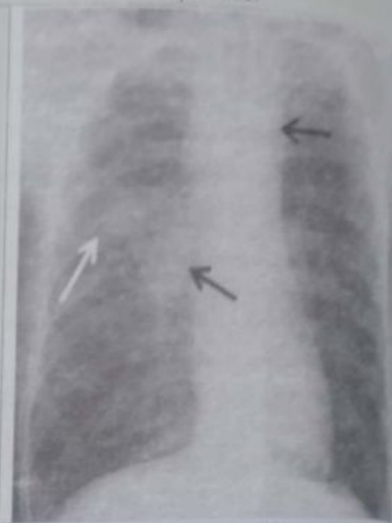
 - » Inj. Linezolid 600mg/300ml (Nezkil, Ecasil) x IV x BD
 - » OR Inj. Vancomycin 500mg x IV x TDS
- » **Indication for interventional therapy:** large or complicated lung abscess, significant hemoptysis, do not respond to antibiotic therapy alone, complications (e.g., sepsis, respiratory distress), or those causing compression of adjacent structures.
- » **Interventional options:** First line: Bronchoscopic drainage or image-guided percutaneous drainage. Rarely: surgical resection (segmentectomy, lobectomy, pneumonectomy)



PULMONARY TUBERCULOSIS

Name: _____ Age: _____ Sex: _____ Date: _____
 Temperature: _____ B.P: _____ Pulse: _____ Resp. Rate: _____

- ☛ **Agent:** Free living, Acid-Fast Bacilli (Z-N Stained) with a thick (rich lipid) cell wall
- ☛ **Mode of transmission:** Pulmonary TB, mostly spread via droplet infection.
- ☛ **Pathogen host/source:** predominantly humans (infected person coughs up small droplets containing the bacteria that reaches the terminal alveoli of the uninfected person)
- ☛ **Incubation period:** 2 – 6 weeks
- ☛ **Risk factors:**
 1. Endemic area
 2. Drug abuse and Alcoholism
 3. Malnutrition and Poverty
 4. Pre-existing damage to the lungs: E.g., silicosis, COPD
 5. H/O close contact: E.g., Prisons, hospitals, homeless shelters
 6. Immunocompromised: E.g., HIV, immunosuppressive medications i.e. TNF- α inhibitors, and diabetes
 7. Immunosuppression (TB is considered to be the most common cause of mortality in patients with HIV globally)



X-ray chest showing right upper lobe consolidation (white arrow) and right hilar and mediastinal lymphadenopathy (black arrows)



Clinical features

- ☛ **Constitutional upsets:**
 - » Low grade fever or Pyrexia of unknown origin.
 - » Generalized malaise & Fatigue
 - » Night Sweats
 - » Anorexia.
- ☛ **Pulmonary symptoms:**
 - » Dyspnea
 - » Chronic productive cough (possibly hemoptysis) lasting > 3 weeks
 - » chest pain
- ☛ **Physical exam:**
 - » **Weight loss:** due to high circulating level of TNF- α $\rightarrow$ TNF- α increases basal metabolic rate $\rightarrow$ weight loss)
 - » **Lymphadenopathy**

Chest X-ray finding:

- » Middle or lower lung infiltrate (suggestive of primary infection)
- » Upper lobe infiltrate (suggestive of latent TB reactivation)
- » Consolidation
- » Cavitory lesions
- » Collapse
- » Hilar lymphadenopathy
- » Pleural effusions
- » **Ghon complex:** sequelae of primary TB infection (lobar or perihilar lymph node involvement)

Pathogenesis

Pathogenesis mainly by Delayed type-IV hypersensitivity infection
 Also known as granulomatous inflammation $\rightarrow$ **END RESULT $\rightarrow$ GRANULOMA FORMATION** is caused by a delayed T cell-mediated reaction (i.e., type IV hypersensitivity reaction) that leads to the activation of alveolar macrophages (i.e., epithelioid cells) and their fusion into multinucleated giant cells $\rightarrow$ **Alveolar macrophages** are recruited, which eventually become infected, transporting the microbe to deeper tissues (The infection is usually contained in the lung by formation of caseating granulomas that limit damage to the lungs and bacterial dissemination)

- » **Caseating granulomas:** granuloma with central necrosis that causes a cheese-like appearance
- » Granulomas are formed to "wall off" TB, where it lies dormant (Granuloma is a jail)
- » Granuloma formation is a protective- phenomenon, but granuloma formation destroys normal anatomy of organ.

Interpretation of the PPD test

Diameter of the induration	Considered positive in the following groups
≥ 5 mm, positive	» Suggestive of TB with HIV-positive patients » Recent contact with a TB-infected person » Signs of TB on chest x-ray
≥ 10 mm	Patients with high risk of reactivation i.e Risk factors: » IV drug use/immunocompromised » Homelessness/malnutrition/poverty » Immigration from endemic country » Chronic illness (e.g., diabetes mellitus, kidney or lung disease, malignancy) » Occupation (health care or prison workers)
≥ 15 mm, highly positive	» Suggestive of TB in otherwise healthy person » Always considered positive, even without risk factors

DIAGNOSTIC APPROACH OF TUBERCULOSIS (TB)

1. Screening test for TB:
 - A. Tuberculin skin test (TST) or Purified Protein Derivative (PPD) test or Mantoux Test: Inj tuberculin (purified protein derivative) x 0.1 mL (5 units) x intradermally x ventral surface of the lower arm. The diameter of the induration at the injection site is measured after 48–72 hours (Look for swelling+redness after 48–72 hours)
 - B. Additional screening test:
 - Quantiferon TB Gold (QFT) test (Interferon-gamma (IFN- γ) release assay, commonly known as an IGRA): ELISA test that measures the level of interferon- γ expressed by T cells after coming into contact with synthetic TB-specific peptides. Measures interferon levels released by the patient's immune system in response to TB antigens. Results available within 24 hours.
 - T-spot test: Detects interferon-gamma producing T-cells after stimulating patient's lymphocytes with two kinds of tuberculosis-specific antigens (ESAT-6 and CFP-10).
2. Xpert MTB/RIF assay: Molecular test for tuberculosis (TB). The Gene-Xpert diagnoses TB by detecting the presence of TB bacteria, as well as testing for resistance to the drug Rifampicin (RIF).
3. Diagnostic tests:
 1. Real-time nucleic acid amplification (PCR): Rapidly confirms TB and is considered the first-line diagnostic study
 2. Investigation of choice: Sputum smear microscopy for AFB (Z-N Staining) → 3 early morning samples → pretreatment with NaOH (sputum induced with nebulised hypertonic saline if patient not expectorating)
 3. Gold standard test: Culture
- Alternative investigation:
 - » Bronchoscopy with washings or Broncho-Alveolar-Lavage (BAL) for AFB (via bronchoscopy)
 - » PCR TB DNA investigation of choice for multi-Drug Resistance TB
 - » Gastric washing* (mainly used for children) for AFB
 - » BACTEC TB test system
4. Drug susceptible testing (DST) for drug resistance TB (DR-TB)
5. Baseline test: CBC, ESR, CRP, RFTs, LFTs, Electrolytes and T.B ICT (serology-antibody test –Not recommended for diagnosis)

TREATMENT GUIDELINES

General treatment principles

1. Isolation: Every patient diagnosed with active TB must be isolated until sputum, gastric juices, and urine are negative!
2. After 1 month of ATT mycobacterium is absent from sputum and the patient become non-infective.
3. Restart full treatment if there is an interruption of ≥ 14 days during the intensive phase.
4. First-line ATT is safe during pregnancy and breast feeding as well.
5. Baseline test: CBC, LFTs, BUN/Urea, Creatinine, Electrolytes, should be done before starting ATT. Stop/modify first line ATT when LFTs become raised, more than 3-times from normal value.
6. Monitoring of Drugs therapy
7. Monthly sputum samples for microscopy and culture
8. Monitor drug side effects: renal retention parameters, ophthalmological check-up, ENT, and LFTs

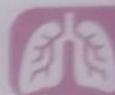
Active Disease

1. Initiation phase: 2 months of "RIPE" – Rifampicin (R), Isoniazid (I), Pyrazinamide (P), Ethambutol (E)
2. Continuation phase: 4 months of isoniazid + rifampin (2DRUGS) x on alternate day
3. WHO Recommendation in Endemic area: Duration of Continous phase can be increased upto 7 months

First-line ATT: Rifampicin (R), Isoniazid (I), Pyrazinamide (P), Ethambutol (E) and/or Streptomycin (S).

FIRST-LINE ANTI-TUBERCULAR DRUGS THERAPY (ATT)

Medication	Daily dose per kg	Three times a week dose	Side-Effects
Rifampicin (R)	10mg (10–20mg) Maximum: 600 mg/dose	15mg/kg Max: 600 mg/dose	Red or orange discoloration body fluids (urine, tears) Hepatotoxic CYP-inducer (especially CYP3A4, CYP2C9)
Isoniazid (I)	5mg (4–6mg/kg) Maximum: 300 mg/dose	15mg/kg Max: 900 mg/dose	Peripheral neuropathy and other symptoms of pyridoxine deficiency (e.g., stomatitis, glossitis, convulsions, and anemia) Hepatotoxicity (acute hepatitis, chronic liver failure)
Pyrazinamide (P)	25mg (20–25mg) Maximum: 2 g/dose	35mg (30–40) mg/kg Max: 2 g/dose	Hepatotoxic, Hyperuricemia → Gout Arthralgia and Myopathy Blood dyscrasias: (↓ Haemoglobin, ↓ Platelets) Contraindicated in Porphyria (haem-metabolism)
Ethambutol (E)	15mg (15–25mg) Maximum: 1.6 g/dose	35mg (25–35) mg/kg Max: 2.4g/dose	Optic neuritis
Streptomycin (S)	15mg (12–18mg)/kg, Maximum dose: 1.5g/day		Ototoxicity, nephrotoxicity



ANTI-TUBERCULER DRUGS AVAILABLE IN PAKISTAN

GENERIC COMPOSITION	AVAILABLE BRAND
Isoniazid 100mg and 300mg	» Tab. Isoniazid, Tab. Niazid
Rifampicin 300mg, 450mg, and 600mg	» Tab. Lederrif, Tab. Rifadin
Ethambutol 400mg	» Tab. Abbutol, Tab. Myambutol, Tab. Schazobutol
Pyrazinamide 500mg	» Tab. Pyrazid » Tab. PZA-Ciba
Rifampicin 300mg + Isoniazid 150mg	» Tab. Rifinah 300mg, Tab. Rifapin-H 450mg » Tab. Rimactal INH 450mg, Tab. Pire-2
Ethambutol 300mg + Isoniazid 100mg	» Tab. Myambutol-INH 300mg » Tab. Rifapin-H 300mg
Ethambutol 400mg + Isoniazid 150mg	» Tab. Myambutol INH Forte 400/150mg » Tab. Schazobutol-H
Rifampicin 150mg + Isoniazid 75mg + Ethambutol 275mg	» Tab. Myrin fort, Tab. Rimthree FDC
Rifampicin 150mg + Isoniazid 75mg + Ethambutol 300mg	» Tab. Myrin, Tab. Rifatol » Tab. Rimcure FDC, Tab. Refine-E, Tab. Pire-3
Rifampicin 150mg + Isoniazid 75mg + Pyrazinamide 400mg	» Tab. Refine-E, Tab. Rifater
Rifampicin 120mg + Pyrazinamide 300mg + Ethambutol 225mg + Isoniazid 60mg	» Tab. Myrin-P, Tab. Rifa-4
Rifampicin 150mg + Isoniazid 75mg + Ethambutol 275mg + Pyrazinamide 400mg	» Tab. Myrin-P Forte, Tab. Rimstar » Tab. Rifin-4, Tab. Pire-4 plus, Tab. Rifa-4 plus
Streptomycin	» Inj. Streptomycin 1g/vial



PULMONARY TUBERCULOSIS (PTB)

Phases of treatment of active PTB:

- » **Intensive phase:** Combination of 4 drugs "RIPE" for 2 months (60 Doses)
- » **Continuation phase:** Combination of 2 drugs "RI" for 4 months (120 Doses)
- » Daily dosing is preferred.
- » **Three times weekly dosing:** an alternative if the patient has no HIV infection and is at low risk for a TB relapse.

Treatment administration

- » Self-administered & daily dosages are preferred
- » **Directly observed therapy (DOT):** Health care personnel observe the patient taking TB drugs

Duration of treatment: 6 months (180 Doses)

Drug-resistant TB is resistant to one first-line antituberculous drug, either isoniazid or rifampin. **Multidrug-resistant TB** is resistant to isoniazid and rifampin, and possibly additional agents. **Extensively drug-resistant TB** is resistant to isoniazid, rifampicin, all fluoroquinolone, and either bedaquiline or linezolid. **Outcomes of drug-resistant TB treatment** are worse than drug-sensitive TB organisms, and outcomes appear to vary with HIV status



(Rifampicin 150mg + Isoniazid 75mg + Ethambutol 275mg + Pyrazinamide 400mg)

1. **Tab. Myrin-P Forte Tab. Pire-4 plus or Tab. Rifa-4 plus**
3-4 tablets before breakfast
Patients should be given the following single daily dose 1-2 hours before a meal, according to patient's body weight.
2. **Tab. Pyridoxine 50mg** (Vita-6, Amdoxine)
0-0-1 (HS) [for the prevention of vitamin B6 deficiency]
3. **Syp. Appetite stimulant/vitamins** (Tresorix fort, Trimetabol)
2-0-2 (Two teaspoonful 30min before meal x twice daily)

Treatment Monitoring

Monthly follow-up of outpatients is recommended, including sputum smear and culture for M tuberculosis at monthly intervals until cultures are negative on two consecutive samples. Patients with negative sputum cultures after 2 months of treatment should have at least one additional sputum smear and culture performed at the end of therapy. Patients with drug-resistant isolates should have sputum cultures performed monthly during the entire course of treatment. A CXR at the end of therapy provides a useful baseline for any future comparison. Patients whose cultures do not become negative or whose symptoms do not resolve despite 3 months of therapy should be evaluated for nonadherence to the regimen and for drug-resistant organisms. DOT is recommended for the remainder of the treatment regimen, and the addition of at least two drugs not previously given should be considered pending repeat drug susceptibility testing. The clinician should seek expert assistance if drug resistance is newly found, if the patient remains symptomatic, or if smears or cultures remain positive. Patients with only a clinical diagnosis of pulmonary tuberculosis (smears and cultures negative for M tuberculosis) whose symptoms and radiographic abnormalities are unchanged after 3 months of treatment usually either have another process or have had tuberculosis in the past. CMDT 2024

BRONCHIAL ASTHMA

- **Asthma:** a respiratory disease that is characterized by chronic airway inflammation and manifests with variable respiratory symptoms and expiratory airflow limitation.
- **Acute asthma exacerbation:** a reversible worsening of the clinical features of asthma that develops over a short period of time and can progress to life-threatening asthma.

TRIGGERS & RISK FACTORS OF ASTHMA

Allergic asthma (extrinsic asthma) – 95%	Non-allergic asthma (intrinsic asthma) – 5%
• Cardinal risk factor: Atopy • Environmental allergens: Pollen (seasonal), dust mites, domestic animals (house rats), mold spores, fumes, fibre, fungal spores, soft furnishings (carpet, curtain, sofa, Cushing) • Allergic occupational asthma from exposure to allergens in the workplace (flour dust)	• Viral respiratory tract infections • Chronic sinusitis or chronic rhinitis, cold air, stress • Physical exertion (laughter, exercise-induced asthma) • GERD: Often exists concurrently with asthma. • Chronic sinusitis or chronic rhinitis • Medication: NSAIDs (Aspirin-Induced Asthma), Beta-Blockers • Irritant-induced asthma: from exposure to solvents, ozone, tobacco or wood smoke, cleaning agents, isocyanates

CLINICAL FEATURES

- Recent upper respiratory tract infection
- Chest tightness, dyspnea, cough with sputum (white)
- **Expiratory wheeze:** whistling sounds from airways.
- **Symptoms of allergic rhinitis:** Repeated sneezing, Runny nose, and Postnasal drip (feeling of mucus secretions moving down the back of the throat)
- **Family history of asthma**
- **Nighttime allergies, and nasal polyposis**
- **Allergen history** (cats, dogs, cockroaches, dust mites, fungal spores, environmental tobacco smoke, fumes from chemicals (e.g., bleach), and pollen from trees, weeds, and grass)
- **Cigarette smoking or Vaping (e-cigarettes) and Drugs allergy**
- **Atopy history:** Eczema, Atopic dermatitis, Allergic rhinitis (70%)
- **On physical Examination:**
 - » **Inspection:** Bilaterally Reduced chest movements
 - » **Palpation:** Bilaterally Reduced chest movements
 - » **Percussion:** Resonant
 - » **Auscultation:** Bilaterally reduced air entry PLUS Rhonchi.

DIAGNOSTIC WORKUP

- **Chest X-ray:** Normal or hyperinflated
- **Spirometry:** ↓ FEV1 and ↓ FEV1/FVC ratio (<80% of predicted value).
- **Peak expiratory flow rate (PEFR):** Flow rate as a comparison to patient's personal best or normal values for height and gender
- **CBC:** norm or ↑ eosinophils &/or neutrophil
- **Allergen specific-IgE tests:** Positive
- **Frictional exhaled nitric oxide (FeNO):** Low: <25 parts per billion (ppb), Intermediate: 25–50 ppb, high: >50 ppb (not recommended)
- **Bronchial challenge test:** Positive
- **Sputum examination:** not done routinely.
 - » Eosinophils ↑ in type-2 inflammation
 - » Churchman spirals
 - » Charcoat laden crystals
- **ABGs:** maybe type-1 Respiratory failure (↓ PaO2, PaCO2 normal)



CLASSIFICATION OF ASTHMA SEVERITY IN ADULTS & ADOLESCENT

Severity	Impairment over the past 4 weeks	Lung function	Exacerbation
Intermittent asthma	• Symptom frequency: ≤2 days a week • Nighttime awakening due to asthma: ≤2 ×/month • No limitation of daily activities • Use of short-acting beta agonist (SABA) ≤2 days/week	• FEV1 normal between exacerbations • FEV1 > 80% of the predicted average value • Normal FEV1/FVC	≤1 ×/year
Mild persistent asthma	• Symptom frequency: 3–6 days/week • Nighttime awakening due to asthma: 3–4 ×/month • Minor limitation of daily activities • Use of SABA 3 days/week to 1 ×/day	• FEV1 ≥ 80% of the predicted average value • Normal FEV1/FVC	≥2 ×/year
Moderate persistent asthma	• Symptom frequency: daily • Nighttime awakening due to asthma: 2–6 ×/week • Some limitation of daily activities • Use of SABA 7 days/week	• FEV1 60–79% of the predicted average value • FEV1/FVC reduced by 5%	
Severe persistent asthma	• Symptoms throughout the day • Nighttime awakening due to asthma: up to 7 ×/week • Extreme limitation of daily activities • Use of SABA several times a day	• FEV1 < 60% of the predicted average value • FEV1/FVC reduced by ≥ 5%	



STEPWISE "GINA 2023" RECOMMENDED TREATMENT OF ASTHMA IN ADULTS & ADOLESCENT

According to available ICS (Inhaled corticosteroids) in Pakistan

- GINA recommends step 1 – 2 treatments as: **Asthma symptoms or need for a reliever twice a month or more (but less than 4-5 days per week):** Low-dose ICS budesonide + formoterol as needed (RPN)
 - ↳ Budesonide 200mcg + Formoterol 6mcg x 1 inhalation/puffs as needed (RPN).
- GINA recommends step 3 treatment as: **Asthma symptoms most days of the week, or waking due to asthma once a week or more, especially if any risk factors exist:** Low-dose ICS budesonide + formoterol as needed (RPN)
 - ↳ Budesonide 200mcg + Formoterol 6mcg x 1 inhalation/puffs once or BD or 1 inhalation/puffs as needed.
 - » Available Inhaler: Foracort HFA Inhaler, Fortide Inhaler x 1 puffs once or twice daily as needed.
 - » Available Dry powder Inhalation (DPI): Venticort 200 rotacaps, Combivair 200 rotacaps, Formigret 200 rotacaps, Symbidow rotacaps x 1 DPI Capsule inhale via DPI device x once or twice daily as needed.
- GINA recommends step 4 treatments such as: **Daily symptoms or waking with symptoms of asthma once a week or more and low lung function:** Medium-dose budesonide/formoterol PLUS as needed (PRN) low-dose budesonide/formoterol.
 - ↳ Budesonide 400mcg + Formoterol 6mcg x 2 inhalations twice daily PLUS 1 inhalation as needed.
 - » Available Dry powder Inhalation (DPI): Venticort 400 rotacaps, Combivair 400 rotacaps, Formigret 400 rotacaps, Symbidow rotacaps x 1 DPI Capsule inhale via DPI device x twice daily as needed.
- GINA recommends step 5 treatment as:
 - ↳ Patient with inadequate symptom relief with step 4 treatment
 - ↳ Encourage adherence to step 4 treatment and consult a specialist to consider:
 - » Trial of high-dose ICS/LABA (Budesonide 800mcg + Formoterol 12mcg) for 3–6 months
 - » Add-on LAMA: Tiotropium bromide 2.5 mcg x inhaled once daily.
 - » Consider additional therapies:
 1. Macrolide: Tab. Azithromycin 500mg (Azomax) x orally three times weekly
 2. Biologics (anti-IgE, anti-IL-5/5R, anti-IL-4R)
 - Inj. Omalizumab: at dose 75mg to 375mg by subcutaneous once every 2 or 4 weeks, Based on serum total IgE level (IU/mL) and patient body weight in kg.
 - Inj. Mepolizumab at dose 100mg subcutaneously every 4 weeks
 - Inj. Reslizumab at dose 3mg/kg IV infusion every 4 weeks
 3. Low-dose oral corticosteroids (Low dose OCS): Tab. Prednisolone 5mg (Deltacortril) x ≤ 7.5 mg orally once daily, most effective in achieving prompt control of asthma during acute exacerbations. Pulse therapy initially at 40 to 60 mg/day in divided doses, tapered to zero during 7 to 14 days. **CMDT-2024**
 - Consider side effects: As oral corticosteroids often lead to substantial adverse effects, patients need to be counseled about and monitored for potential adverse effects, especially if treatment is expected to last 3 months or more. Some patients may need therapy for prevention of osteoporosis.



ALTERNATIVE TREATMENT OPTION FOR CONTROLLING & RELIEVING ASTHMA

Step 1 (intermittent asthma)

- ↳ Daily therapy with single inhalers: usually not required
- ↳ Rescue inhaler (as needed): SABA = Salbutamol Inhaler (Ventolin Evohaler, Salbo HFA Inhaler)
 - » 2 puffs every 4–6 hours as needed
 - » 2 puffs 5 minutes before exercise

Step 2 (Mild Persistent Asthma)

- ↳ Daily therapy with single inhalers: Low dose ICS = Beclomethasone 250mcg (Clenil Inhaler, Bekson Inhaler)
 - » Adjust dose to achieve asthma control with a dose of 2 puffs twice daily
- ↳ Rescue inhaler (as needed): SABA = Salbutamol (Ventolin Evohaler, Salbo HFA Inhaler)
 - » 2 puffs every 4–6 hours as needed
 - » 2 puffs 5 minutes before exercise
- ↳ OR Rescue ICS + SABA only = Beclomethasone + Salbutamol (Clenil Compositum, Xaltide HFA Inhaler)
 - » 2 puffs three or four times daily
- ↳ PLUS, Leukotriene receptor antagonists (LTRAs) → Tab. Montelukast 10mg (Mytika, Montiget) x OD (HS)

Step 3 (Moderate Persistent Asthma)

- ↳ Low-dose ICS + Formoterol (daily and rescue therapy) = Salmeterol 25mcg + Fluticasone 50mcg

- » Brands: Seretide Evohaler, Saltra Inhaler, Salmicort HFA Inhaler
- » 2 puffs twice daily, titrate up and down as symptom control requires.
- » Max dose is 4 puffs of highest strength per day.

➤ **PLUS, Leukotriene receptor antagonists (LTRAs):** Tab. Montelukast 10mg (Mytika, Montiget) x OD (H5)

Step 4 (moderate to severe persistent asthma)

➤ Medium dose ICS + Formoterol (daily and rescue therapy) = **Budesonide 200mcg + Formoterol 6mcg**

- » Inhaler: Foracort HFA Inhaler, Fortide Inhaler
- » Dry powder Inhalation (DPI): Venticort 200 rotacap, Combivair 200 rotacap Formiget 200 rotacap
- » 2 puffs twice daily or 1 DPI Capsule inhale via DPI device twice daily, depends on severity of asthma.

➤ **PLUS, Leukotriene receptor antagonists (LTRAs):** Tab. Montelukast 10mg (Mytika, Montiget) x OD (H5)

Step 5 (severe persistent asthma)

➤ Daily therapy with single inhalers: Medium-to high-dose ICS-LABA + LAMA (Tiotropium bromide DPI)

Step-4 treatment to medium dose PLUS LAMA (Tiotropium bromide DPI)

➤ **Salmeterol 25mcg/Fluticasone 125mcg**

- » Brands: Seretide 25/125mcg Evohaler, Saltra 25/125mcg Inhaler, Salmicort 25/125mcg HFA Inhaler
- » 2 puffs twice daily, titrate up and down as symptom control requires. Max dose is 4 puffs per day.

➤ **OR Budesonide 400mcg + Formoterol 12mcg**

- » Dry powder Inhalation (DPI): Venticort 400 rotacap, Combivair 400 rotacap Formiget 400 rotacap.
- » 1 DPI Capsule inhale via DPI device twice daily, depends on severity of asthma, titrated upto 4 times.

➤ **PLUS, Tiotropium bromide 18mcg DPI Capsule** (Tioget, Tioveez, Gentrop 18mcg DPI Capsule)

1 DPI Capsule Inhale once-daily, with the Respomatic (DPI device) at the same time of the day.

Do not take more than one dose in 24 hours.

➤ Rescue inhaler (as needed): SABA (see step-1)

Step 6 (severe persistent asthma) (Oral Prednisolone or IV methylprednisolone)

➤ Daily therapy with single inhalers: High-dose ICS-LABA, PLUS Corticosteroids ↗

➤ **Salmeterol 25mcg/Fluticasone 250mcg**

- » Brands: Seretide 25/250mcg Evohaler, Saltra 25/250mcg Inhaler, Salmicort 25/250mcg HFA Inhaler
- » 2 puffs twice daily, titrate up and down as symptom control requires. Max dose is 4 puffs per day.

➤ **OR Budesonide 400mcg + Formoterol 12mcg**

- » Dry powder Inhalation (DPI): Venticort 400 rotacap, Combivair 400 rotacap Formiget 400 rotacap.
- » 1 DPI Capsule inhale via DPI device twice daily, depends on severity of asthma, titrated upto 4 times.

➤ **PLUS Tab. Prednisolone 5mg** (Deltacortril) x ≤ 7.5 mg orally once daily OR **IV methylprednisolone** most effective in achieving prompt control of asthma during acute exacerbations. Pulse therapy initially at 40 to 60 mg/day in divided doses, tapered to zero during 7 to 14 days. CMDT-2024

➤ Rescue inhaler (as needed): SABA (see step-1)

NON-PHARMACOLOGICAL MANAGEMENT FOR ASTHMA

- **Smoking cessation:** Strongly encourage quitting at every consultation; provide access to counseling/programs.
- **Physical activity:** Regular exercise benefits lung function, asthma control, and quality of life; use maintenance ICS to reduce exercise-induced bronchoconstriction.
- **Avoid occupational exposures:** Refer to a specialist for suspected/confirmed occupational asthma; eliminate sensitizers and remove patients from exposure.
- **Medication avoidance:** Avoid aspirin and NSAIDs if there's a history of reactions; beta-blockers should be prescribed case-by-case by a specialist.
- **Healthy diet:** Eat a diet high in fruits and vegetables for overall health.
- **Avoid indoor allergens:** Not generally recommended; remove mold and dampness to improve symptoms.
- **Avoid outdoor allergens:** Stay indoors with windows and doors closed during high pollen/mold counts; use AC
- **Weight reduction:** Weight loss improves outcomes in obese patients; bariatric surgery is more effective than nonsurgical methods.
- **Breathing exercises:** May help but require more research.
- **Avoid indoor air pollution:** Use non-polluting heaters and cookers; avoid smoking and passive smoke.
- **Avoid outdoor air pollution:** Stay indoors during cold weather, low humidity, or high pollution; avoid polluted environments during infections.
- **Manage emotional stress:** Find strategies to manage stress; assess mental health for anxiety or depression.
- **Avoid certain foods:** Avoid confirmed food allergens to reduce exacerbations.



CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

- » Symptoms are minimal or non-specific until the disease reaches an advanced stage.
- » Presenting findings
 - » Chronic cough with expectoration (expectoration typically occurs in the morning)
 - » Dyspnea and tachypnea
 - » Initial stages: Only on exertion SOB and tachypnea.
 - » Advanced stages: Continuously SOB and tachypnea.
 - » Pursed lip breathing
 - » The patient breathes in through the nose and breathes out slowly through pursed lips.
 - » This style of breathing increases airway pressure and prevents bronchial collapse during the last phase of expiration.
 - » More commonly seen in patients with emphysema
 - » Prolonged expiratory phase, end-expiratory wheezing, crackles, muffled breath sounds, and/or coarse rhonchi on auscultation
 - » Cyanosis due to hypoxemia
 - » Tachycardia
- » Features of advanced COPD
 - » Congested neck veins
 - » **Barrel chest:** This deformity is **most commonly** seen in individuals with emphysema.
 - » Asynchronous movement of the chest and abdomen during respiration
 - » Use of accessory respiratory muscles due to diaphragmatic dysfunction
 - » Hyperresonant lungs, reduced diaphragmatic excursion, and relative cardiac dullness on percussion
 - » **Decreased breath sounds on auscultation:** "silent lung"
 - » Peripheral edema (most often ankle edema).
 - » Right ventricular hypertrophy with signs of right heart failure and cor pulmonale
 - » Hepatomegaly
 - » Often weight loss and cachexia
 - » Secondary polycythemia
 - » **Confusion:** due to hypoxemia and hypercapnia
 - » Nail clubbing in the case of certain comorbidities (e.g., bronchiectasis, pulmonary fibrosis, lung cancer)

PINK PUFFER AND BLUE BLOATER

	Pink Puffer	Blue Bloater
Main Pathomechanism	Emphysema	Chronic bronchitis
Features	Non-cyanotic Cachectic Pursed-lip breathing Mild cough	Productive cough Overweight Peripheral edema
Chest X-ray	Hyperinflated lung & tubular heart	Dirty lung 'prominent vasculature'
CBC	Hb Normal, TLC Increased	Hb increased, TLC Normal
Pao ₂	Slightly reduced	Markedly reduced
PaCo ₂	Normal (possibly in late hypercapnia)	Increased (early hypercapnia)
Respiratory failure	Type-1	Type-2

Investigation of choice → Pulmonary function test (PFT)

Spirometry and/or body plethysmography

- » FEV₁/FVC < 70%
- » Decreased FEV₁
- » Normal or decreased FVC
- » Increased FRC and RV
- » Total Leucocyte count (TLC)
 - » Chronic bronchitis: normal
 - » Emphysema: increased
- » Increased intrathoracic gas volume
- » Transfer factor for carbon monoxide (DLCO)
 - » Chronic bronchitis: normal
 - » Emphysema: decreased

Postbronchodilator test

- » Objective: assesses reversibility of bronchoconstriction
- » Procedure
 - Spirometry to establish a baseline
 - Inhalation (e.g., salbutamol)
 - Perform spirometry again after = 10–15 min.
- » Results: FEV₁/FVC < 0.7 is diagnostic of COPD (in patients with typical clinical features and exposure to noxious stimuli)
 - Delta FEV₁ < 12% (irreversible bronchoconstriction): COPD is more likely than asthma.
 - Delta FEV₁ > 12% (reversible bronchoconstriction): Asthma is more likely than COPD
 - If spirometry is normal, COPD can be excluded.



MANAGEMENT OF COPD

1. General treatment

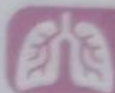
- ☞ **Cessation of tobacco use:** single most effective step to slow the decline in lung function
- ☞ **Pneumococcal vaccination:** reduces the incidence of community-acquired pneumonia and invasive pneumococcal diseases
 - » **Age 19-64 years:** Administer PPSV23 (23-valent pneumococcal polysaccharide vaccine)
 - » **Age ≥ 65 years**
 - **Vaccinated:** Administer PPSV23 (should be at least 5 years after the previous PPSV23 dose and at least 1 year after PCV13).
 - **Not vaccinated or unknown vaccination history:** Administer PCV13 followed by PPSV23.
 - **Immunocompetent patients:** Administer PPSV23 after 1 year.
 - **Individuals with immunocompromising conditions, cerebrospinal leaks, or cochlear implants:** Administer PPSV23 after 8 weeks.
- ☞ **Influenza vaccination (annual):** Reduces the incidence of lower respiratory tract infections and death in COPD patients
- ☞ **Pulmonary rehabilitation**
 - » Indicated in patients with GOLD-B, C, and D
 - » Includes physiotherapy with breathing exercises
- ☞ Physical activity helps maintain endurance and alleviate dyspnea.
- ☞ Supportive treatment (e.g., postural drainage)
- ☞ Supplementation with Vitamin D and calcium in cases of deficiency

2. Medical treatment according to GOLD

- ☞ Medical treatment in COPD reduces the severity of symptoms, improves overall health status, and lowers the frequency and severity of exacerbation.
- ☞ The first-line treatment of COPD consists of bronchodilators, inhaled corticosteroids, and phosphodiesterase (PDE) type 4 inhibitors.
 - » **Bronchodilators**
 - ☞ **Short-acting beta agonists (SABAs):** Salbutamol
 - ☞ **Long-acting beta agonists (LABAs):** Salmeterol, formoterol
 - ☞ **Short-acting muscarinic antagonists (SAMAs):** Ipratropium bromide
 - ☞ **Long-acting muscarinic antagonists (LAMAs):** Tiotropium bromide
 - » **Inhaled corticosteroids (ICS):** Budesonide, fluticasone, Beclomethasone
 - » **PDE type 4 inhibitors (PDE4i)**
 - ☞ **Tab. Roflumilast 500mcg (Milast, Romilast) x 250mcg for 4 weeks then 500mcg x OD**

TREATMENT GUIDELINES OF COPD

Patient group	Exacerbations per year	Symptoms	Initial treatment	Subsequent Escalation/2 nd line
A	» ≤1 (with no hospital admission)	Mild symptoms	» SABA (Salbutamol, Albuterol) » Or SAMA (Ipratropium bromide) ^{Best}	» Continue or combination therapy SABA + SAMA
B		Severe symptoms	» LABA or LAMA	» LABA + LAMA
C	» ≥2 » ≥1 leading to hospital admission	Mild symptoms	» ICS + LABA or LAMA	» LAMA + LABA (preferred) » Or PDE4i + LABA or LAMA
D		Severe symptoms	» ICS + LABA and/or LAMA » If highly symptomatic (CAT >20): LAMA + LABA (preferred) » Consider LABA and ICS in patients with high eosinophil count	» Triple therapy with LAMA + LABA + ICS » Consider adding PDE4i: if FEV ₁ < 50% predicted and chronic bronchitis » Consider adding macrolide (Azithromycin) in former smoker » Consider stopping ICS (due to possible adverse effects such as pneumonia)



3. OTHER TREATMENT OPTIONS FOR COPD

- ☞ Theophylline (Tab. Theogard 300mg, Cap. Respro SR 200mg)
 - » Mechanism of action: adenosine receptor blockade and nonspecific PDE inhibition
 - » Indication: usually only severe and refractory COPD
- ☞ Long-term oxygen therapy (LTOT) indicated in the case of:
 - » $\text{PaO}_2 \leq 55 \text{ mm Hg}$ or $\text{SaO}_2 \leq 88\%$ at rest
 - Increases the chance of survival in patients with COPD
 - Supplemental O_2 can worsen hypercapnia
 - The target oxygen saturation is 90–93%.
 - » PaO_2 between 55 and 60 mmHg or SaO_2 of 88%, if there is evidence of pulmonary hypertension, congestive cardiac failure, or polycythemia
- ☞ Mucolytics (e.g., N-Acetylcysteine) liquefy mucus by reducing the disulfide bonds of mucoproteins.
 - » N-Acetylcysteine 200mg sachets (Mucolator) x TDS in 1 cup water, or dilute in 5–10ml water x Nebulize 2–3ml every 2 to 4 hourly.
- ☞ Ventilatory support: CPAP is useful in patients with COPD and obstructive sleep apnea.
- ☞ Surgery may be beneficial in severe cases
 - » Lung resection for giant bullae in emphysema
 - » Lung transplantation for nonrepairable damage
- ☞ Bronchoscopic interventions may be used to reduce end-expiratory lung volume and improve exercise tolerance.



TREATMENT OF COPD

- ☞ Avoidance of Smoking: single most effective and important step to slow the decline in lung function
- ☞ Supplemental oxygen therapy for patients with resting hypoxemia ($\text{PaO}_2 < 56 \text{ mmHg}$) is the only therapy with evidence of improvement in the natural history of COPD. Proven benefits of home oxygen therapy in hypoxemic patients include longer survival, reduced hospitalization and better quality of life.
Administer oxygen at flow rate 1–3L/minute through nasal cannula to achieve a PaO_2 of 60 to 70 mmHg OR an SaO_2 between 88% and 92%
- ☞ Pulmonary Rehabilitation, Physiotherapy and Vaccination.

MILD COPD SYMPTOMS

- ☞ SABA = Salbutamol inhaler (Ventolin Evohaler, Salbo HFA Inhaler)
 - » 2 puffs every 4–6 hours as needed
- ☞ OR/PLUS SAMA = Ipratropium bromide Inhaler (Atrovent Inhaler, Atem Inhaler, Optra Inhaler)
 - » 2 to 4 puffs every six hours per day

MODERATE COPD SYMPTOMS

- ☞ LAMA = Tiotropium bromide 18mcg DPI Capsule (Tioget, Tioveez, Gentrop 18mcg DPI Capsule)
 - » 1 DPI Capsule Inhale once-daily, with the Respomatic (DPI device) at the same time of the day.
 - » Do not take more than one dose in 24 hours.
- ☞ SABA = Salbutamol inhaler (Ventolin Evohaler, Salbo HFA Inhaler)
 - » 2 puffs every 4–6 hours as needed
- ☞ If not controlled than add on Inhaled corticosteroids (ICS)
 - » Beclomethasone 250mcg (Clenil 250mcg inhaler, Bekson Fort 250mcg Inhaler)
 - » Fluticasone (Flixotide Evohaler)

SEVERE SYMPTOMS

- ☞ ICS + LABA = Salmeterol 25mcg/Fluticasone 250mcg
 - » Brands: Seretide 25/250mcg Evohaler, Saltra 25/250mcg Inhaler, Salmicort 25/250mcg HFA Inhaler
 - » 2 puffs twice daily, titrate up and down as symptom control requires. Max dose is 4 puffs per day.
- ☞ OR/PLUS LAMA = Tiotropium bromide 18mcg DPI Capsule (Tioget, Tioveez, Gentrop 18mcg DPI Capsule)
 - » 1 DPI Capsule Inhale once-daily, with the Respomatic (DPI device) at the same time of the day.
 - » Do not take more than one dose in 24 hours.
- ☞ Tab. Roflumilast 500mcg (Milast, Romilast)
 - » 0–0– $\frac{1}{2}$ for 4 weeks than one daily (250mcg x OD for 4 weeks than 500mcg x OD)

Prescribe antibiotics in moderately or severely ill patients if there is evidence of infection, such as change in volume of sputum and increased purulence of sputum or Respiratory tract infection

- ☞ Tab. Azithromycin 500mg (Azomax, Zetro) x OD OR Tab. Levofloxacin 500mg (Leflox, Cravit) x OD for 5–7 days

SEVERE COUGH IN PATIENT WITH HISTORY OF ASTHMA

Name:
Temperature:Age:
B.P.:Sex:
Pulse:Date:
Resp. Rate:△
c/c:

- » Postnasal drop
- » Cough
- » Hypersecretion
- » Sputum production
- » Shortness of breath
- » Wheezing
- » Sneezing
- » Chest pain

Diagnostic workup

- » Chest X-ray
- » CBC
- » PFTs
- » Sputum culture
- » Sputum gram staining
- » If long duration chronic cough
Order Sputum for AFB

Fexofenadine should be used with caution along with Azithromycin because combination will increased the risk of QT prolongation

Rx

Prescription - 01

1. **Ipratropium bromide Nebulization** (Atrovent, Atem)
Diluted in 2ml 0.9% N/S every 6-8 hourly.
I - I - I - I (QID) OR I - I - I (TDS)
2. **Betamethasone + Salbutamol Nebulization** (Clenil compositum)
Dilute in 2ml 0.9% N/S every 6-8 hourly
I - I - I - I (QID) OR I - I - I (TDS)
3. **Tab. Cetirizine 10mg** (Zyrtec, Rigix)
OR **Tab. Loratidine 10mg** (Softin, Lormax)
I - 0 - I (OD)
4. **Antibiotics usually not required, consider, if RTI:**
 - ☞ **Tab. Co-Amoxiclav** (Augmentin) 625mg x TDS, OR 1g x BD
I - I - I (625mg = TDS) OR I - 0 - I (1g = BD) for 7-10 days
 - OR **Tab. Azithromycin 500mg** (Azomax, Zetro) x OD for 5 days
5. **Cough suppressants for symptomatic relief:**
 - ☞ **Syp. Cofrest** x 2 Teaspoonful (10ml) x TDS
 - ☞ OR **Syp. Corex-D** x 2 Teaspoonful (10ml) x TDS
 - ☞ OR **Syp. Ivy leaf** x (Coferb) x 2 Teaspoonful (10ml) x TDS

Rx

Prescription - 02

1. **Ipratropium bromide Nebulization** (Atrovent, Atem)
Diluted in 2ml 0.9% N/S every 6-8 hourly.
I - I - I - I (QID) OR I - I - I (TDS)
2. **Betamethasone + Salbutamol Nebulization** (Clenil compositum)
Dilute in 2ml 0.9% N/S every 6-8 hourly.
I - I - I - I (QID) OR I - I - I (TDS)
3. **Tab. Montelukast sodium 10mg** (Monitiget, Mytika, Singulair)
0 - 0 - I (OD)
4. **Tab. Ebastine 10mg OR Tab. Ebastine 20mg** (Kestine)
OR **Tab. Fexofenadine 60mg, 120mg, 180mg** (Telfast, Fexet, Fexo)
0 - 0 - I (OD)
5. **Antibiotics usually not required, consider, if in patient with RTI:**
 - Tab. Levofloxacin 500mg** (Leflox, Cravit)
 - OR **Tab. Moxifloxacin 400mg** (Moxiget, Avelox)
 - OR **Tab. Clarithromycin 500mg XL** (Klaricid XL, Claritek XL)
0 - 0 - I (OD) for 5-10 days
6. **Cough suppressants for symptomatic relief:**
 - ☞ **Syp. Pulmonol** x 2 Teaspoonful (10ml) x TDS
 - ☞ OR **Syp. Seroline** x 2 Teaspoonful (10ml) x TDS
 - ☞ OR **Syp. Cofrest** x 2 Teaspoonful (10ml) x TDS
 - ☞ OR **Syp. Ivy leaf** x (Coferb) 2 Teaspoonful (10ml) x TDS

If not respond than consider oral corticosteroids: **Tab. Prednisolone** (Deltacortril, Rapicort) at dose of 40 to 60 mg/day in 2-3 divided doses, tapered to zero during 7 to 14 days, is recommended.



PLEURAL EFFUSION

Name: _____ Age: _____ Sex: _____ Date: _____
 Temperature: _____ B.P: _____ Pulse: _____ Resp. Rate: _____

ETIO-PATHOGENESIS OF PLEURAL EFFUSION

Transudative pleural effusion	Exudative pleural effusion
Protein: < 3g/dl Pathophysiology: » ↑ Capillary hydrostatic pressure (↑ capillary wedge pressure) » ↓ Capillary oncotic pressure Common causes of Transudative pleural effusion » ↑ Capillary hydrostatic pressure ▪ Congestive heart failure (CHF) ▪ Hypothyroidism ▪ Cardiac tamponade ▪ Meig's syndrome » ↓ Capillary oncotic pressure ▪ Hepatic cirrhosis ▪ Nephrotic syndrome ▪ Protein-losing enteropathy ▪ Chronic kidney disease (Na⁺ retention)	Protein: > 3g/dl Pathophysiology: ↑ Capillary permeability (due to inflammation) Common causes of Exudative pleural effusion » Infection: Pneumonia (parapneumonic effusion), Tuberculosis, Pleural empyema, amebiasis » Malignancies: Lung cancer, Metastatic breast CA, Lymphoma, Mesothelioma and Ovarian CA » Pulmonary embolism (PE) » Autoimmune disease (especially collagen vascular diseases): Vasculitis, SLE, Rheumatoid arthritis, Sarcoidosis and scleroderma » Trauma (high vascular permeability) » Acute Pancreatitis » Hemothorax » Chylothorax and Pseudochylothorax

Differentiating transudates from exudates PLUS Including Light criteria

Laboratory parameters		Transudative effusion	Exudative effusion
Light criteria	» Pleural fluid protein/serum protein ratio	≤ 0.5	> 0.5
	» Pleural fluid LDH/serum LDH ratio	≤ 0.6	> 0.6
	» Pleural fluid LDH	< ⅔ the upper limit of normal serum LDH	> ⅔ the upper limit of normal serum LDH
**Very high pleural LDH levels >1000 U/L, suggest empyema, malignancy, or rheumatoid effusion			
Pleural fluid cholesterol		< 45 mg/dL	> 55 mg/dL
Pleural fluid LDH		< 200 U/L	> 200 U/L
Pleural fluid cholesterol : serum cholesterol ratio		< 0.3	> 0.3

Clinical features	Radiological Investigation
Symptoms » Patients with a small pleural effusion (< 300 mL) are often asymptomatic. » Characteristic symptoms: ▪ Dyspnea/shortness of breath ▪ Pleuritic chest pain (sharp retrosternal pain) ▪ Non-productive, dry cough » Symptoms of the underlying disease (Fever in empyema, cachexia in cases of malignancy, symptoms of left-sided heart failure) Physical exam findings » Inspection and palpation: Asymmetric expansion and Unilateral lagging on the affected side, Reduced tactile fremitus due to fluid in the pleural space » Auscultation: Faint or absent breath sounds over the area of effusion. Pleural friction rub (squeaking sound of inflamed pleural layers rubbing together during inspiration and expiration) » Percussion: dullness over the area of effusion	Chest X-ray (CXR) P.A view (Investigation of choice) » Mild pleural effusion: 200-250ml fluid, blunting of cardiophrenic and costophrenic angles. » Moderate pleural effusion: 500ml fluid, homogenous white opacity, having a concavity upward. If having straight border think of hydro-pneumothorax. » Massive pleural effusion: 1000ml fluid, white out lung – Complete opacification of the lung – Mediastinal shift – Tracheal deviation away from the effusion (space-occupying lesion) Chest X-ray lateral view: 50ml fluid Chest X-ray decubitus view: >10ml fluid USG chest: detect fluid amounts as low as 20 mL (>10ml) Gold-standard investigation: HRCT (detect >3-5ml fluid)

Laboratory Investigation

- » CBC: anemia, infection (WBCs ↑)
- » Serum NT-Pro-BNP: (↑) >125 pg/mL < 75, >450 pg/mL >75 years of age (suggestive of Heart failure)
- » LFTs: May be abnormal
- » Serum Albumin and Protein: ↓
- » Serum LDH and serum protein
- » Abnormal Coagulation Profile
- » Inflammatory markers: CRP & ESR
- » Proteinuria → Nephrotic syndrome
- » Serum TSH: ↑ (Hypothyroidism)
- » Pleural fluid analysis

Therapeutic thoracentesis: The goal of a therapeutic thoracentesis is to remove fluid (especially in exudate because of increased risk of infection). Removal of 400–500 mL of fluid is usually sufficient to relieve symptoms (Dyspnea).

» Indications

- » Large effusion with dyspnea and/or cardiac decompensation
- » Complicated parapneumonic effusions

» Contraindications

- » There are no absolute contraindications.
- » Relative contraindication: infection over the puncture site (e.g., cellulitis, herpes zoster)

» Complications

- » Vascular injury and hemothorax
- » Pneumothorax
- » Infection (Pleuritis, Empyema)

» Consider diagnostic thoracentesis with for patients with:

- » Signs of increased work of breathing
- » Hypoxemic respiratory failure
- » Hypercapnic respiratory failure
- » Hemodynamic compromise secondary to the effusion

Rx

TREATMENT OF PLEURAL EFFUSION

- » Stabilize patients with respiratory distress & provide supplemental oxygen
- » Perform Diagnostic thoracentesis with pleural fluid analysis
- » Repeat Chest X-ray (CXR) after thoracentesis
- » Consider specialized procedures and/or surgical options after specialist adv
- » Identify and treat the underlying condition.
 - » Manage heart failure/pulmonary edema: Inj. Furosemide (Lasix) at dose 40–80mg x IV x STAT, Followed by oral Tab. Lasix 20–40mg x OD
 - » Collagen vascular diseases: IV corticosteroids
 - » Nephrotic syndrome: Manage underlying renal disease.
 - » Manage pancreatitis: See surgery portion "Acute pancreatitis"
 - » Pancreaticopleural fistula: Endoscopic or surgical intervention
 - » Meigs syndrome: Removal of ovarian tumor is recommended.
 - » Pulmonary Embolism: Anticoagulation therapy.
 - » Malignancy: targeted cancer immunotherapy, chemotherapy, radiotherapy, or surgical resection
- » Consider pleural biopsy for further investigation: (for example: suspected tuberculosis, malignant disease).
- » Consider indwelling pleural catheter placement or pleurodesis for malignant or recurrent effusion.
- » Parapneumonic effusion: Treatment same as pneumonia/CAP – see above
- » Pleural empyema: start IV Empiric antibiotics for pleural infection
 - » All patients should receive empiric antibiotics adjusted to their needs, local resistance patterns, and institutional guidelines.
 - » Community-acquired pleural empyema
 - » Combination therapy with Inj. Ceftriaxone 2g (Oxidil) x IV x OD PLUS, one of the following: Inj. Metronidazole 500mg/100ml (Flagyl) x IV x TDS OR Inj. Clindamycin 600mg/4ml (Dalacin-C) x 20–40mg/kg/day x TDS
 - » OR SINGLE-AGENT THERAPY WITH IV Inj. Co-Amoxiclavate 1.2g (Augmentin) x IV x BD OR Inj. Ampicillin-sulbactam 1.5g to 3g (Ambac) x IV x every 6 hour (QID)
 - » Hospital-acquired pleural empyema:
 - » Inj. Vancomycin 500mg x IV x TDS
 - » PLUS, ONE of the following:
 - Inj. Cefepime 1g x BD + Inj. Metronidazole 500mg x IV x TDS
 - Inj. Piperacillin-tazobactam 4.5g (Tanzo, Tazocin EF) x IV x TDS
 - Inj. Meropenem 1g (Meronem, Penro) x IV x TDS (if extended-spectrum β-lactamase-producing organisms are suspected)



X-ray chest (PA view): There is marked homogeneous opacification (green overlay) of the middle and lower aspects of the left hemithorax from pleural effusion and passive atelectasis of adjacent lung tissue. The margins of the left hemidiaphragm and left heart are obscured. A concave upper lateral border, or meniscus (white arrow/white dashed line), helps confirm the presence of effusion.

SARCOIDOSIS

Clinical features

- General: fever, malaise, loss of appetite, weight loss, lymphadenopathy
- Pulmonary: dyspnea of insidious onset, cough, chest pain
- Extrapulmonary: arthritis, erythema nodosum, anterior uveitis, lupus pernio, peripheral neuropathy, cardiomyopathy
- Mediastinal lymph nodes: bilateral, hilar, and/or paratracheal mediastinal adenopathies (in 90% cases)
- Physical findings of interstitial lung disease with crackles are uncommon.
- Other findings may include parotid gland enlargement, hepatosplenomegaly, and lymphadenopathy.

Diagnostic workup

- Best initial: Chest x-ray – Reveals bilateral hilar lymphadenopathy with or without pulmonary infiltrates (i.e., reticular and/or ground glass opacities). Radiographic stages include bilateral hilar adenopathy alone (radiographic stage I), hilar adenopathy and parenchymal involvement (radiographic stage II), parenchymal involvement alone (radiographic stage III), or advanced fibrotic changes principally in the upper lobes (radiographic stage IV).
- High-resolution CT (HRCT) – Characteristic HRCT appearances include reticulonodular opacities that follow a perilymphatic distribution centred on bronchovascular bundles and the subpleural areas.
- Pulmonary function testing (PFTs): may show a restrictive defect accompanied by impaired gas exchange with early reduction of Diffusing capacity of the lung for carbon monoxide (DLCO) and lung compliance.
- Obtained laboratory test:
 - CBC and differential: Leukopenia
 - Inflammatory markers: Elevated serum ESR & serum CRP
 - Serum calcium: Elevated (Hypercalcemia) due to elevated 1,25-dihydroxy-vitamin-D
 - Serum 1,25-OH and 25-OH vitamin-D levels obtained in patients with hypercalcemia
 - BUN & creatinine: Elevated, may indicate tubulointerstitial disease
 - Alkaline phosphates (ALP) &/or GGT: Elevated (>3 x ULN), may indicate hepatic involvement
 - Urinalysis: hypercalciuria
 - Serum IgG: Elevated
 - Serum ACE levels: ↑ in 40–80% cases with active disease, though this finding is neither sensitive nor specific.
 - TB screening: interferon-γ release assay, tuberculin skin tests
- Additional investigation:
 - 12-lead ECG: concerning findings include heart block, frequent PVCs, tachyarrhythmias.
 - TTE for pulmonary hypertension screening if ↓ DLCO or if enlarged pulmonary artery is present on HRCT
 - Bronchoscopy may demonstrate a 'cobblestone' appearance of the mucosa
 - Bronchoalveolar lavage fluid typically contains an increased CD4:CD8 T-cell ratio.
 - Cardiac MRI is favored over FDG-PET scan for patients with suspected cardiac involvement (cardiac sarcoidosis)
- Gold standard diagnostic: Biopsy and histopathology, Biopsy of easily accessible sites (e.g., superficial palpable lymph nodes, skin lesions, or salivary glands) may be an initial step → Histopathological Finding: Non-caseating granulomas with giant cells, Asteroid bodies, Schaumann bodies.



TREATMENT OF SARCOIDOSIS

- First-line is Glucocorticoids: Tab. Prednisolone 5mg at dose 20–40mg per day, can be withheld for 6 months. Topical glucocorticoids may be useful in cases of mild uveitis, and inhaled glucocorticoids have been used to shorten the duration of systemic glucocorticoid use in asymptomatic parenchymal sarcoidosis
- Consider DMARD: If no response severe disease or adverse effects to glucocorticoids (Prednisolone)
 - Tab. Methotrexate (Unitrexate) at dose 10–20mg/week (preferred choice) or Tab. Azathioprine 50mg (Immunon) at dose 50–150mg/day (alone or with prednisolone)
 - Tumour necrosis factor alpha (TNF-α) inhibitors
 - Tab. Chloroquine or Tab. Hydroxychloroquine
 - Low-dose thalidomide may be useful in cutaneous sarcoidosis with limited pulmonary involvement.
- Supportive and preventive treatment:
 - Prevent complications of glucocorticoids therapy and adverse effects of immunosuppressants.
 - Provide individualized supportive care: NSAIDs for pain relief, noninvasive ventilation, supplemental oxygen
 - Patients should be warned that strong sunlight may precipitate hypercalcaemia and endanger renal function.
 - Transplantation: Selected patients may be referred for consideration of single lung transplantation.
 - The overall mortality is low (1%–5%) and usually reflects cardiac involvement or pulmonary fibrosis.

BRONCHIECTASIS

Definition: Bronchiectasis means abnormal dilatation of the bronchi. Chronic suppurative airway infection with sputum production, progressive scarring and lung damage occurs, whatever the cause.

CLINICAL FEATURES

- ❑ **Chronic, daily, persistent cough** (Lasting months to years) with copious amount continuous purulent sputum
- ❑ **Hemoptysis** (usually mild or self-limiting), Streaks of blood common, larger volumes with exacerbations of infection
- ❑ **Pleuritic chest pain:** when infection spreads to involve pleura, or with segmental collapse due to retained secretions.
- ❑ **Halitosis:** frequently accompanies purulent sputum
- ❑ **Nonspecific symptoms:** Rhinosinusitis, dyspnea, fatigue, malaise, weight loss, pallor due to anemia
- ❑ **On physical examination:**
 - » **Auscultation:** Crackles and rhonchi, Wheezing (due to obstruction from secretions, airway collapsibility, or a concomitant condition) and bronchophony
 - » **Clubbing of nails** (uncommon)
 - » **Cyanosis**
- ❑ **Exacerbations of bronchiectasis:** increased sputum volume with fever, malaise, anorexia
 - » Recurrent bouts of pneumonia and acute bacterial infection of sections of dilated bronchi
 - » Frequently due to *Pseudomonas aeruginosa*
 - » **Features:** Increased production of mucous above baseline, Low-grade fever

DIAGNOSTIC WORKUP

- ❑ **Best initial chest test:** Chest X-ray – Mild bronchiectasis may not be apparent on a plain chest X-ray.
- ❑ **Confirmatory test:** HRCT chest (High-resolution computed tomography chest) – **Gold standard**
 - Radiological finding**
 - » Fibrocystic changes
 - » **Cylindrical or tubular (most common):** parallel tram track sign and signet ring sign
 - » Saccular or cystic (most severe form)
 - » Thickened bronchial walls, mucus plugging, honeycombing (suggests late-stage bronchiectasis)
 - » Perihilar lymphadenopathies
- ❑ **Complete blood count (CBC):** Decrease Hb, Increased WBCs, Increased thrombocytes.
- ❑ **Consider ABGs (e.g., in patients with ↓ SaO₂ on room air):** may show hypercapnia
- ❑ **Sputum culture and smear:** May reveal *Pseudomonas aeruginosa* and *Staphylococcus aureus*, fungi such as *Aspergillus* and non-tuberculous mycobacteria.
- ❑ **Spirometry:** not needed to establish a diagnosis but useful to monitor disease progression

**TREATMENT OF ACUTE EXACERBATIONS OF BRONCHIECTASIS**

- ❑ Provide supportive treatment and oxygen therapy as needed.
- ❑ **Physiotherapy:** involves daily exercises to help drain excess bronchial secretions, reducing cough, sputum, and infections. Patients should position the affected lobe uppermost and use deep breathing followed by forced expiratory maneuvers. Various devices, like positive expiratory pressure masks or flutter valves, may aid in sputum clearance. The best technique varies per individual. Generally, 5-10 min twice daily is recommended.
- ❑ Optimize mucoactive agents and airway clearance techniques
- ❑ Obtain a new sputum culture and start empiric antibiotic therapy, based on the most recent sputum culture.
- ❑ Tailor antibiotics to the most recent sputum culture once available & preferably complete 14 days of therapy.
 - ❖ **No previous culture data available:**
 - Consider fluoroquinolones**
 - » **Tab. Levofloxacin 500mg** (Leflox) x Once daily (OD)
 - » **OR Tab. Ciprofloxacin 500mg** (Hiflox, Novidat, Ciproxen) x Twice daily (BD)
 - » **OR Tab. Moxifloxacin 400mg** (Moxiget, Avelox) x Once daily (OD)
 - ❖ **Previous culture data and antibiogram available**
 - Colonization with sensitive pathogens**
 - » **Tab. Amoxicillin/clavulanic acid** (Augmentin 625mg) x Three times daily (TDS)
 - » **OR Tab. Azithromycin 500mg** (Zetro, Azomax) x Once daily
 - » **OR Tab. Clarithromycin XL 500mg** (Claritek XL, Klaricid XL) x Once daily (OD)
 - » **OR Cap. Doxycycline 100mg** (Vibramycin, Doxyn) x Twice daily (BD)
 - » **OR Cap. Cefadroxil 500mg** (Duricef, Cedrox) x Twice daily (BD)



LONG-TERM MANAGEMENT OF BRONCHIECTASIS

Management goals are to stop or delay disease progression, reduce exacerbation frequency (goal ≤ 2 per year), achieve symptom control, and improve the patient's quality of life.

- ☞ Educate the patient regarding prognosis and the use of long-term medications.
- ☞ Promote lifestyle changes like regular exercise and avoidance of smoking/tobacco use
- ☞ Educate the patient on airway clearance techniques
 - » **Bronchopulmonary hygiene and chest physiotherapy:** e.g., cupping and clapping, postural drainage, directed cough and oral hydration
 - » **Pulmonary rehabilitation:** may improve exercise capacity and respiratory symptoms
- ☞ Administer vaccinations (i.e., seasonal influenza vaccine, pneumococcal vaccine).
- ☞ Consider treatment with mucoactive agents, bronchodilators, or corticosteroids if airway clearance is difficult.
- ☞ Provide specific treatment for the underlying cause if identified.
- ☞ **Follow-up:** Perform follow-ups every 6–12 months to identify disease progression.
- ☞ **Bacterial and fungal sputum culture:** every 6–12 months
- ☞ **Mucoactive agents:** Consider in patients with difficulty expectorating or persistent symptoms despite adequate airway clearance techniques; continue use based on clinical benefits.
 - » **Nebulized mucoactive agents:** Trial for at least 3 months.
 - Hypertonic saline (3–7% NaCl)
 - Mannitol
 - » **Oral mucolytics:** Trial for at least 6 months
 - N-acetylcysteine (Mucolator 200mg sachets) in a cup water x BD/TDS
 - Syp. Carbocisteine 250mg/5ml (Rhinathiol, Carbex)
- ☞ **Bronchodilators:** Consider on a case-by-case basis. Evidence to support the use of bronchodilators in bronchiectasis is limited.
 - » **Short-term bronchodilators (SABA, SAMA):** in patients with airway reactivity and bronchospasm or prior to inhaled mucoactive treatment.
 - **SABA = Salbutamol inhaler** (Ventolin Evohaler, Salbo HFA Inhaler)
2-puffs every 4–6 hours as needed
 - **OR/PLUS SAMA = Ipratropium bromide Inhaler** (Atrovent Inhaler, Atem Inhaler, Optira Inhaler)
2 to 4 puffs every six hours per day
 - » **Long-term bronchodilators (LABA, LAMA):** may be used in patients with severe dyspnea
 - » **Regular use of bronchodilators (e.g., for asthma or COPD):** Continue as usual.
- ☞ **Corticosteroids:** Corticosteroids are not routinely recommended because of the limited benefit and side effects of corticosteroid therapy. (See above Asthma/COPD)
 - » **Inhaled corticosteroids (ICS):** Continue if already indicated for asthma or COPD
 - » **Systemic corticosteroids:** indicated in patients with Allergic bronchopulmonary aspergillosis (ABPA)
- ☞ **Long-term antibiotic therapy:** The goal is to suppress bacterial growth & to reduce symptoms & exacerbations as a measure of secondary prevention in patients with ≥ 3 exacerbations per year. Antibiotic therapy should be administered for at least 3 months and may be extended based on clinical response and tolerability.
 - » **First-line:** Low-dose oral macrolide therapy (Azithromycin 500mg three times per week or 250 mg/day)
 - **Tab. Azithromycin 500mg** (Azomax, Zetro, Macrobac) x every alternate day (three times per week)
 - **OR Cap. Azithromycin 250mg** (Azomax, Azitma, Macrobac) x Once daily
 - » **Alternative:** inhaled antibiotics such as Gentamicin 80mg x twice daily Or Tobramycin 300mg x BD
 - » **Nontuberculous mycobacteria:** Treatment usually includes three drugs (macrolide PLUS rifampicin PLUS ethambutol) for at least one year.
 - » **MRSA:** Consider eradication therapy based on local hospital protocols

Invasive procedures for Bronchiectasis

- ☞ **Surgical resection of bronchiectatic lung or lobectomy:** indicated in pulmonary hemorrhage, inviable bronchus, and poor control of symptoms despite optimal medical therapy in unilateral bronchiectasis with well-localized disease
- ☞ **Pulmonary artery embolization:** indicated in pulmonary hemorrhage
- ☞ **Lung transplantation:** Consider for severe disease or rapid disease progression.



EVALUATION OF CARCINOMA LUNG (BRONCHOGENIC CARCINOMA)

- Pulmonary symptoms:** Persistent cough (often dry) most common early symptoms followed by, Progressive dyspnea, > Chest pain, > Hemoptysis (coughing up blood or bloody mucus, **Major source:** bronchial arteries).
 - Slightly more common on right side, more frequently occurs in upper lobes
 - Endobronchial growth** of central tumors cause cough, stridor, wheeze and dyspnoea
 - Peripheral tumors** present as pain due to pleural or chest wall involvement
- Extrapulmonary symptoms**
 - Constitutional symptom:** unintentional weight loss, fever, fatigue, weakness.
 - Clinical features of tumor infiltration and/or compression of neighboring structures
 - SVC syndrome:** due to compression of the superior vena cava (SVC) impairs the venous backflow to the right atrium, resulting in venous congestion in the head, neck, and upper extremities. (MC cause is SCLC > SCC)
 - Hoarseness:** due to paralysis of recurrent laryngeal nerve (RLN)
 - Dyspnea and diaphragmatic elevation:** due to paralysis of the phrenic nerve
 - Malignant pleural effusion** on the affected side, **Dullness on percussion, reduced breath sounds**
 - Bronchial obstruction:** May causes pneumonia or lung abscess
 - Esophageal compression:** Causes difficulty swallowing (dysphagia).
 - Pancoast syndrome:** involvement of C8-T1 nerves by pancoast tumor causing pain in ipsilateral shoulder & arm
 - Recurrent respiratory infections** (e.g., pneumonia, bronchitis) in the same pulmonary region in patients ≥ 40 years old should always raise suspicion for lung cancer.
- Symptoms of metastatic disease:** Over half of all patients diagnosed with lung cancer have metastatic disease at the time of presentation. The symptoms of metastatic disease are site-specific
 - Brain:** Headaches, seizures, focal motor deficits, behavioral changes
 - Liver:** Typically asymptomatic, but may manifest with nausea, jaundice, ascites
 - Adrenal gland:** Typically, asymptomatic
 - Bones:** Bone pain, Elevated serum alkaline phosphatase (ALP) and Elevated calcium

4. Paraneoplastic syndromes

- | | |
|--|---|
| <ul style="list-style-type: none"> CVS: Thrombophlebitis migrans, Non-bacterial thrombotic endocarditis (NBTE), also known as Libman-Sacks endocarditis Metabolic: <ul style="list-style-type: none"> Syndrome of inappropriate antidiuretic hormone secretion (SIADH) – Small cell lung carcinoma (SCLC) Hypercalcemia of malignancy: increased risk with SCC. Acanthosis nigricans (adenocarcinoma), Dermatomyositis, Icthyosis, Erythema gyratum repens, Cachexia. Hypertrophic osteoarthropathy: Clubbing, periostitis, Arthritis | <ul style="list-style-type: none"> GIT: Carcinoid syndrome Erythrocytosis, Thrombocytosis Neuromuscular: <ul style="list-style-type: none"> Dementia, optic neuritis Retinopathy, limbic encephalitis Autonomic neuropathy (SCLC) Lambert-Eaton syndrome (SCLS) Polymyositis, cerebellar degeneration. Gynecomastia due to production of hCG |
|--|---|

5. Metastases (Spread)

- Most common site of metastasis:** Brain > Bone > Liver > Adrenal > Lung (BB-LAL)
- CA lung is most common primary for metastasis to** Kidney, Esophagus, Pancreas, Adrenal, Brain & Skin (KEPABS).

Diagnostic workup

- Chest x-ray PA view:** First line and initial step to evaluate cough, chest pain, and/or hemoptysis.
- CT chest:** indicated in all patients with an abnormal chest x-ray or suspicion of carcinoma lung
- Confirmation of diagnosis:** Biopsy and histopathology → Histopathological analysis of tissue biopsies is required to confirm the diagnosis of lung cancer; cytology may be confirmatory in select cases.
- Obtaining samples:** Less invasive methods are preferred.
 - Pulmonary lesions**
 - Central:** bronchoscopy with transbronchial biopsy
 - Peripheral:** needle aspiration guided by endobronchial ultrasound or CT
 - Pleural effusion:** thoracentesis with cytology of the effusion; pleural biopsy if cytology is negative
 - Metastasis to other organs (e.g., mediastinum, lymph nodes):** percutaneous or surgical biopsy, bone marrow biopsy if there is suspected bone marrow infiltration
- Advanced investigation for carcinoma lung staging:** CT thorax and abdomen, MRI brain with gadolinium enhancement or CT brain with contrast and PET-CT to assess bone metastases
- CBC:** May detect anemia, neutropenia, and/or thrombocytopenia
- Alkaline phosphatase (ALP):** Elevated, may indicate bone &/or liver metastasis
- Liver function test (LFTs):** Abnormal, may indicate liver metastasis
- Serum calcium:** Elevated (Hypercalcemia) may indicate bone metastasis or paraneoplastic syndrome
- LDH:** possibly elevated

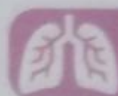


COMMONLY USED MEDICATIONS IN RESPIRATORY DISEASES

Drug class	Generic name	Brand name
Short-acting beta-2 agonists (SABA)	Salbutamol	» Ventolin 100mcg Evohaler
		» Salbo 100mcg HFA Inhaler
		» Ventolin 5mg (0.5%) nebulizer solution
		» Tab. Ventolin 2mg, Tab. Ventolin 4mg
		» Inj. Ventolin 0.5mg/ml
		» Breavent 200mcg ROTACAPS
Long-acting beta-2 agonists (LABA)	Levalbuterol	» LEVHALE 0.63mg/3ml
		» LEVHALE 1.25mg/3ml
	Terbutaline	» Syp. Britanyl 0.3mg/ml
		» Tab. Britanyl 2.5mg
		» Inj. Britanyl 0.5mg/ml
	Salmeterol	» Available in combination with ICS
	Formoterol	
Inhaled corticosteroids (ICS)	Tulobuterol	» Syp. Bremax 1mg/5ml
		» Tab. Bremax 1mg, Tab. Bremax 2mg
	Bambuterol	» Tab. BTno 10mg, Tab. BTno 20mg
		» Tab. Pulmitec 10mg, Tab. Pulmitec 20mg
		» Syp. Pulmitec 5mg/5ml, Syp. BTno 5mg/5ml
	Beclomethasone	» Clenil 250mcg inhaler
Oral corticosteroids		» Bekson Fort 250mcg Inhaler
		» Bekson 50mcg Inhaler
	Budesonide	» Budefrom 100mcg HFA Inhaler
		» Budefrom 200mcg HFA Inhaler
	Fluticasone	» Flixotide Evohaler
	Mometasone	» Asmanax HFA
Parenteral corticosteroids	Dexamethasone	» Tab. Kanadex 5mg
	Prednisolone	» Tab. Deltacortril 5mg
		» Tab. Rapicort 5mg
	Betamethasone	» Tab. Betnesol 0.5mg
		» Tab. Betnelan 0.5mg
	Hydrocortisone NA succinate	» Inj. Solucortif 100mg/vial, 250mg/vial
ICS PLUS SABA (combination inhaled corticosteroid and Short-acting beta-2 agonist)	Dexamethasone	» Inj. Decadron 4mg/ml
	Betamethasone	» Inj. Betnesol 4mg/ml
	Methylprednisolone acetate	» Depo-Medrol 40mg/ml, 80mg/2ml
	Methylprednisolone succinate	» Solu-Medrol 125mg, 500mg, 1000mg/vial
	Beclomethasone 100mcg + Salbutamol 50mcg	» Xaltide 100/50mcg HFA Inhaler
	Beclomethasone and Salbutamol	» Clenil compositum 100/50mcg HFA Inhaler
ICS PLUS LABA (combination inhaled corticosteroid and long-acting beta-2 agonist)		» Breavent-B 100/200mcg ROTACAPS
		» Breavent-B 200/400mcg ROTACAPS
	Beclomethasone 250mcg + Salbutamol 100mcg	» Xaltide HFA 250/100mcg HFA Inhaler
		» Clenil compositum 250/100mcg HFA Inhaler
	Beclomethasone 0.8mg + Salbutamol 1.6mg	» Clenil compositum Nebulizer solution
	Salmeterol 100mcg + Beclomethasone 50mg	» Salnon HFA Inhaler 50/100mg Inhaler
ICS PLUS LABA (combination inhaled corticosteroid and long-acting beta-2 agonist)	Beclomethasone + Formoterol	» Foster 100/6 Inhaler
		» Foster 200/6 Inhaler
	Salmeterol 25 + Fluticasone 50	» Seretide 25/50mcg Evohaler
		» Saltra 25/50mcg HFA Inhaler
		» Salmicort 25/50mcg HFA Inhaler
	Salmeterol 25 + Fluticasone 125	» Seretide 25/125mcg Evohaler
		» Saltra 25/125mcg HFA Inhaler
ICS PLUS LABA (combination inhaled corticosteroid and long-acting beta-2 agonist)	Salmeterol 25 + Fluticasone 125	» Salmicort 25/125mcg HFA Inhaler
	Salmeterol 25 + Fluticasone 250	» Saltra 25/250mcg HFA Inhaler



		» Saltra 25/250mcg HFA Inhaler » Salmicort 25/250mcg HFA Inhaler » Foracort-100 HFA
	Budesonide 100mcg + Formoterol 6mcg	
	Budesonide 200mcg + Formoterol 6mcg	» Foracort-200 HFA Inhaler » Fortide 200 HFA Inhaler » Venticort 200 rotacap » Combivair 200 rotacap » Formiget 200 rotacap
	Budesonide 400mcg + Formoterol 12mcg	» Venticort 400 rotacap » Combivair 400 rotacap » Formiget 400 rotacap
ICS + LABA + Anticholinergic (Glycopyrronium)	Beclomethasone + Formoterol + Glycopyrronium	» Trimbow 87/5/9 inhaler » Trimbow 10/6/12.5 inhaler
Leukotriene receptor antagonists (LTRAs)	Montelukast	» Tab. Mytika 4mg, 5mg and 10mg » Tab. Montika 4mg, 5mg, and 10mg » Tab. Aerokast 4mg, 5mg, and 10mg » Tab. Singulair 4mg, 5mg, and 10mg » Available Sachets: 4mg and 5mg
Short-acting muscarinic antagonists (SAMA)	Ipratropium bromide	» Atem 250mcg/2ml nebulizer solution » Atrovent 500mcg/2ml nebulizer solution » Tropum 250mcg/2ml nebulizer solution » EASHALE 250mcg/2ml nebulizer solution » Ipneb 250mcg/1ml nebulizer solution » Optra HFA 20mcg Inhaler » Optra HFA 40mcg Inhaler » Sprahelar 20mcg Inhaler » Sprahelar 250mcg/2ml solution
Long-acting muscarinic antagonists (LAMA)	Tiotropium bromide DPI = Dry Powder Inhalation	» Tioflow 18mcg DPI Capsule » Tiovair 18mcg DPI Capsule » Tioget 18mcg DPI Capsule » Tioveez 18mcg DPI Capsule » Spiriva Respimat 2.5mcg Inhaler spray » Spiriva Respimat 1.25mcg Inhaler spray
Methylxanthines	Theophylline	» Tab. Theograd 200mg, Tab. Theograd 350mg » Cap. Respro SR 200mg, Cap. Respro SR 300mg » Tab. Quibron-T SR 300mg
	Doxofylline	» Tab. Unifyline 400mg » Syp. Unifyline 100mg/5ml
	Bamifylline	» Tab. Bamifix 600mg
	Aminophylline	» Tab. Phyllocontin 225mg » Inj. Aminophylline
	Roflumilast 500mcg	» Tab. Milast 500mcg » Tab. Raxus 500mcg » Tab. Romilast 500mcg
Other medication	Pirfenidone 200mg	» Tab. Perfinox 200mg » Tab. Perfenex 200mg » Tab. Mac-Fenid 267mg
	Indacaterol	» Cap. Onbrez 150mg » Cap. Onbrez 300mg
	Indacaterol maleate, Glycopyrronium	» Indibro 110/50Mcg DPI capsule » Indyco 110/50Mcg DPI capsule » Ultibro breezhelar 110/50Mcg DPI capsule
	N-Acetyl cysteine (NAC)	» Mucolator 200mg sachets » Fluimucil-A 200mg sachets
	Erdosteine	» Cap. Dostin 150mg, Cap. Dostin 300mg » Syp. Dostin 175mg/5ml, Dostin 225mg sachets



COMMONLY USED ANTI-TUSSIVE/COUGH SUPPLEMENT

Brand Name	Combination Formula
Syp Corex-D	Chlorpheniramine (Maleate), Ephedrine, Dextromethorphan, Sodium Citrate
Syp Bronochol	Ammonium Chloride, Chlorpheniramine, Ephedrine, Menthol, Potassium Bicarbonate, Potassium Guaiacol sulphate, Senega, Terpin Hydrate
Syp Babynol	[Chlorpheniramine (Maleate): 1mg/5ml, Dextromethorphan: 7mg/5ml]
Syp Seroline	Theophylline + Diphenhydramine + Ammonium Chloride + Menthol
Syp Pulmonol	Ammonium Chloride, Chlorpheniramine (Maleate), Ephedrine, Ipecac, Menthol, Potassium Bicarbonate, Potassium Guaiacol sulphate, Potassium Salts, Senega, Terpin Hydrate
Syp Cofrest	Ammonium Chloride, Diphenhydramine, Menthol, Theophylline
Syp Acefyl cough	Acefyllin Piperazine, Diphenhydramine
Syp Hydryllin	Aminophylline, Ammonium Chloride, Diphenhydramine, Menthol
Syp Hydryllin DM	Dextromethorphan hydrobromide, Diphenhydramine hydrochloride
Syp Reltus	Ammonium Chloride, Chlorpheniramine Maleate, Ephedrine
Syp Reltus DM	Dextromethorphan, Chlorpheniramine maleate, Pseudoephedrine
Syp Cosom	Dextromethorphan Hydrobromide, Pseudoephedrine Hydrochloride, Chlorpheniramine Maleate
Syp Cosom-E	Aminophylline, Ammonium Chloride Containing Expectorants
Syp Combinol-E	Aminophylline, Diphenhydramine, Ammonium Chloride and Menthol
Syp Combinol-D	Dextromethorphan Hydrobromide, Ephedrine Hydrochloride, Chlorpheniramine Maleate, Terpin Hydrate, Ammonium Chloride
Syp Combinol Junior	Promethazine, Pholcodine
Syp Adalin	Aminophylline, Diphenhydramine, Ammonium Chloride, Menthol
Syp Actifed DM	Triprolidine, Dextromethorphan, Pseudoephedrine
SUGAR FREE COUGH SYRUP	
Syp Adicos sugar free	Diphenhydramine, Aminophylline, Ammonium Chloride, Menthol
Syp Hydryllin Sugar free	Aminophylline, Diphenhydramine, Ammonium Chloride, Menthol
Syp Pacific's DM	Dextromethorphan, Chlorpheniramine Maleate, Pseudoephedrine HCl
Syp Coferb	Ivy leaf extract
Syp Olcup	
Syp Coferb plus	Ivy leaf Ivy leaf extract with Thyme and Licorice
Syp Samvy plus	





EVALUATION TO THE MANAGEMENT OF HYPERTENSION

1. **Definition:** Hypertension, defined as a systolic blood pressure > 120 mmHg or a Diastolic blood pressure > 80 mmHg, occurs in 20% to 40% of the population. Hypertension is diagnosed when you have two or more elevated blood pressure readings at least a week apart.

The 2017 American College of Cardiology (ACC)/American Heart Association (AHA) guidelines define it as a blood pressure of $\geq 130/80$ mmHg and by Eighth Joint National Committee (JNC-8) criteria as $\geq 140/90$ mmHg.

2. **TYPES OF HYPERTENSIONS:**

- » **Primary (Essential) hypertension:** =90% of cases of hypertension & has no detectable cause (idiopathic)
- » **Secondary hypertension:** Occurs secondary to another disease process (e.g., renal, endocrine disorder and vascular diseases) in approximately 5% to 10% of patients.

3. **Clinically, hypertension is usually asymptomatic** until organ damage occurs, which commonly affects the brain, heart, kidneys, and/or eyes (e.g., retinopathy, myocardial infarction, stroke). If present, early symptoms of hypertension may include headache, dizziness, tinnitus, and chest discomfort.

AHA/ACC 2017 B.P Categories

B.P Category	Systolic blood pressure (mm Hg)	Diastolic blood pressure (mm Hg)
Normal blood pressure	< 120 mm Hg	< 80 mm Hg
Elevated	$120 - 129$ mm Hg	< 80 mm Hg
Stage 1 hypertension	$130 - 139$ mm Hg	$80 - 89$ mm Hg
Stage 2 hypertension	≥ 140 mm Hg	≥ 90 mm Hg

JNC-8 B.P categories

BP Category	Systolic blood pressure (mm Hg)	Diastolic blood pressure (mm Hg)
Normal blood pressure	< 120 mm Hg	< 80 mm Hg
Pre-Hypertension	$120 - 139$ mm Hg	$80 - 89$ mm Hg
Stage 1 hypertension	$140 - 159$ mm Hg	$90 - 99$ mm Hg
Stage 2 hypertension	≥ 160 mm Hg	≥ 100 mm Hg

GENERAL APPROACH

- ☞ Screen patients using in-office blood pressure (OBP) measurement.
- ☞ Confirm elevated values with Ambulatory BP measurement (ABPM) OR Home BP monitoring (HBPM)
- ☞ **Perform a thorough physical examination and obtain initial laboratory studies.**
 - » Stratify patients by cardiovascular risk (using the ASCVD risk estimator tool).
 - » Evaluate for target organ damage.
- ☞ **Consider diagnostic workup for secondary causes of hypertension in patients with:**
 - » Abnormalities identified during evaluation for newly diagnosed hypertension.
 - » Signs suggestive of secondary hypertension.

SCREENING FOR HYPERTENSION

- ☞ **Indications**
 - » **Annual screening**
 - Individuals > 40 years of age
 - Adults of any age with risk factors for primary hypertension
 - » **Screening every 3 to 5 years:** Individuals 18 to 39 years of age with PREVIOUSLY NORMAL BLOOD PRESSURE ($< 130/85$ mmHg) and no risk factors
- ☞ **Method:** In-office blood pressure measurement
 - » If elevated, measurements should be repeated on both arms.
 - » Elevated average blood pressure on at least two readings obtained on at least two separate visits supports a diagnosis of hypertension.



CONFIRMATION OF HYPERTENSION

- ☞ Out-of-office measurement is recommended in all individuals for confirmation of hypertension before initiating treatment.
 - » Ambulatory blood pressure measurement (ABPM): Preferred method.
 - » Takes measurements while the individual is carrying out normal activities during the day & at nighttime
- ☞ Home blood pressure monitoring (HBPM): Blood pressure is measured by the individual at periodic intervals.

NICE GUIDELINES 2019 FOR DIAGNOSIS OF HYPERTENSION

- ☞ When considering a diagnosis of hypertension, measure blood pressure in both arms:
 - » If the difference in readings between arms is more than 15 mmHg, repeat the measurements.
 - » If the difference in readings between arms remains more than 15 mmHg on the second measurement, measure subsequent blood pressures in the arm with the higher reading.
- ☞ If blood pressure measured in the clinic is 140/90 mmHg or higher:
 - » Take a second measurement during the consultation.
 - » If the second measurement is substantially different from the first, take a third measurement
 - » Record the lower of the last 2 measurements as the clinic blood pressure.
- ☞ If clinic blood pressure (CBP) is between 140/90 mmHg and 180/120 mmHg, offer ambulatory blood pressure monitoring (ABPM) to confirm the diagnosis of hypertension.
- ☞ If ABPM is unsuitable or the person is unable to tolerate it, offer home blood pressure monitoring (HBPM) to confirm the diagnosis of hypertension.
- ☞ When using ABPM to confirm a diagnosis of hypertension, ensure that at least 2 measurements per hour are taken during the person's usual waking hours (for example, between 08:00 and 22:00).
 - » Use the average value of at least 14 measurements taken during the person's usual waking hours to confirm a diagnosis of hypertension (While waiting for confirmation of a diagnosis of hypertension, advise investigation to rule out other causes)
- ☞ When using HBPM to confirm a diagnosis of hypertension, ensure that:
 - » For each blood pressure recording, 2 consecutive measurements are taken, at least 1 minute apart and with the person seated and
 - » Blood pressure is recorded twice daily, ideally in the morning and evening and
 - » Blood pressure recording continues for at least 4 days, ideally for 7 days
- ☞ Discard the measurements taken on the first day and use the average value of all the remaining measurements to confirm a diagnosis of hypertension.
- ☞ Confirm Diagnosis of Hypertension in people with a:
 - » Clinic blood pressure of 140/90 mmHg or higher and
 - » ABPM daytime average or HBPM average of 135/85 mmHg or higher

INITIAL WORKUP IN NEWLY DIAGNOSED HYPERTENSIVE PATIENT

- ☞ Stratification of cardiovascular risk: Blood sugar & lipid profile (HDL, LDL, & triglycerides) – 12 hours fasting
- ☞ Evaluation of end-organ damage and underlying causes
 - » BUN/Urea, serum creatinine and serum electrolytes.
 - » Serum TSH (If abnormal obtained T4)
 - » Serum uric acid and calcium level
 - » Urine analysis: Proteinuria, hematuria (signs of glomerular injury)
 - » If Diabetic: FBS, RBS, HBA1C, Fasting Lipid profile and Urine for micro-albumin
 - » ECG: LVH, signs of cardiac ischemia (e.g., ST depressions or elevations)
 - » Echocardiography: LVH
 - » Chest x-ray: to rule out cardiomegaly, pulmonary edema
 - » Consider CT Brain – if neurological symptoms are present.

OUTPATIENT APPROACH TO THE MANAGEMENT OF HYPERTENSION

Indications for Anti-Hypertensive treatment: The thresholds for pharmacological treatment are controversial. The following recommendations are based on the 2017 ACC/AHA guidelines.

- ☛ Adults with Systolic BP ≥ 130 mmHg OR Diastolic BP ≥ 80 mmHg and ≥ 1 of the following:
 - ☛ Clinical Atherosclerotic cardiovascular disease (ASCVD): Ischemic heart disease (IHD), peripheral artery disease (PAD), or previous stroke
 - ☛ Congestive heart failure (CHF)
 - ☛ 10-year ASCVD risk $\geq 10\%$; (based on the ACC/AHA Pooled Cohort Equations; includes age ≥ 65 years and diabetes mellitus)
- ☛ All adults with Systolic BP ≥ 140 mmHg or Diastolic BP ≥ 90 mmHg

Choice of initial medication should be based on the following:

- ☛ Patient's initial Blood pressure:
 - » Systolic BP 130 – 139 mmHg OR Diastolic BP 80–89 mmHg (Stage-1 Hypertension): Consider initial monotherapy → Begin therapy with ONE primary antihypertensive agent.
 - » Systolic BP ≥ 140 mmHg OR Diastolic BP ≥ 90 mmHg AND an average blood pressure $> 20/10$ mm Hg above target ($> 160/100$ mmHg) → Begin therapy with TWO primary antihypertensives.
- ☛ Life style modifications for all patients with SBP > 120 mmHg or DBP > 80 mmHg

CHOICE OF ANTI-HYPERTENSIVE MEDICATION

☛ ALL OTHER PATIENT AGE < 55 YEARS:

1. First-line treatment:
 - ☛ ACE inhibitor: Lisinopril, Captopril, Enalapril, Ramipril
 - OR ARB: Valsartan, Telmisartan, Losartan, Candesartan
 - OR CCB: Amlodipine, Nifedipine
 - OR Thiazide diuretic: Hydrochlorothiazide (HTZ)
2. Second-line treatment:
 - ☛ Vasodilating beta-blockers: Carvedilol, Labetolol, Nebivolol

☛ ALL OTHERS PATIENT AGE > 55 YEARS:

1. First-line treatment:
 - ☛ CCB: Amlodipine, Nifedipine
 - OR Thiazide diuretic: Hydrochlorothiazide (HTZ)
2. Second-line:
 - ☛ ACE inhibitor: Lisinopril, Captopril, Enalapril, Ramipril
 - OR ARB: Valsartan, Telmisartan, Losartan, Candesartan
 - OR Vasodilating beta-blockers: Carvedilol, Labetolol, Nebivolol

☛ If BP not respond to single therapy advice combine drugs: ACEI or ARB + CCB or Diuretics (Thiazide)

- ☛ Tab. Amlodipine + Valsartan (Exforge, Newday, Dioplus)
- ☛ OR Tab. Amlodipine + Perindopril (Amlod-P, Coversam)

☛ If not controlled with Combine two drugs (ACEI/ARB + CCB), add Diuretics (Thiazide)

- ☛ Tab. Amlodipine + Valsartan + Hydrochlorothiazide (Exforge-HCT, Avsar Plus, Co-Extor)

☛ For Resistant hypertension: Uncontrolled Hypertension with three classes of anti-hypertensive drugs and the drug should include 'Thiazides',

- ☛ For example PATIENT ON ACEI/ARB + CCB + THIAZIDES and BP still not controlled then ADD ALPHA-BLOCKER OR VASODILATING BETA BLOCKER

☛ In adults with chronic kidney disease (CKD): Initial (or Add-On) treatment should include an ACE inhibitors or ARBs to improve kidney outcome.

☛ Do not combine an ACE inhibitor with an ARB to treat hypertension (NICE-2019)



Strategies for initial management of hypertension

Rx

ALL OTHERS PATIENT, AGE <55 YEARS

1. Lifestyle modifications for managing hypertension

- ☞ A diet rich in fruits, vegetables, and low-fat dairy foods and low in saturated and total fats (DASH diet) has been shown to lower blood pressure. Increased dietary fiber lowers blood pressure
- ☞ Decrease dietary sodium: Daily salt intake < 1500 mg
- ☞ ↑ Dietary Potassium: Daily potassium intake 3.5 – 5g (preferably by increasing fruit & vegetable intake)
- ☞ Decrease alcohol intake, provide counseling on alcohol use disorder, if necessary.
- ☞ Daily Regular Exercise: 20 – 25 minutes per day or 150 minutes per week
- ☞ Weight loss: Target BMI is 18.5 – 24.9
- ☞ Smoking cessation should be advised in all patients to reduce ASCVD risk.



2. Choice of Anti-Hypertensive Agent:

- ☞ First-line treatment: ACE inhibitor or ARB or CCB or diuretic
- ☞ Second-line treatment: Vasodilating Beta blockers

ACEIs based treatment	OR ARBs based treatment
☞ Tab. Lisinopril 5mg or 10mg (Zestril) » Initial oral dose 5mg upto 10mg x Once daily » Dosage range: 5–40mg x Once daily	☞ Tab. Valsartan 80mg, 160mg, 320mg (Exforge, Diovan) » Initial oral dose 80mg x Once daily » Dosage range: 80–320mg x Once daily
☞ OR Tab. Enalapril 5mg or 10mg (Renitec, Cortec) » Initial oral dose 5mg x Once daily » Dosage range: 5–40mg in 1 or 2 doses	☞ OR Tab. Telmisartan 20mg, 40mg (Telsarta, Tasmil) » Initial oral dose 40mg x Once daily » Dosage range: 40–80mg x Once daily
☞ OR Tab. Captopril 25mg or 50mg (Capoten, Capril) » Initial oral dose 25mg x Twice daily » Dosage range: 50–450mg in 2 or 3 doses	☞ OR Tab. Losartan 50mg or 100mg (Eziday, Cozaar) » Initial oral dose 50mg x Once daily » Dosage range: 50mg up to 100mg x Once daily

Rx

ALL OTHERS PATIENT, AGE > 55 YEARS

1. Lifestyle modifications for managing hypertension (as mention Above)

2. Choice of Anti-Hypertensive Agent

- ☞ First line: CCB OR Diuretic
- ☞ Second line: ACE inhibitors OR ARB OR vasodilating beta-blocker
- ☞ Tab. Amlodipine 5mg or 10mg (Norvasc, Sofvasc)
 - » Initial dose 2.5 mg x once daily
 - » Dosage range: 2.5 mg upto 10 mg x once daily
- ☞ OR Tab. Nifedipine 30mg (Adalat LA)
 - » Initial dose 30 mg x once daily
 - » Dosage range: 30 mg – 90 mg ER x once daily



If BP does not respond to single drug advice combine drugs (ACEI or ARB + CCB or Thiazide Diuretic)

1. Lifestyle modifications for managing hypertension (as mentioned above)

2. Choice of Anti-Hypertensive Agent

- ✎ Amlodipine + Valsartan 5/80mg or 5/160mg or 10/160mg (Exforge, Newday, Diovan, Extor)
 - » Initial oral dose 5mg/80mg upto 5mg/160mg x Once daily
 - » Dosage range: 5mg/80mg upto 10/320mg x Once daily
- ✎ OR Amlodipine + Perindopril 4mg/5mg, or 4mg/10mg or 8mg/5mg or 8/10mg (Coversam, Amlod-P)
 - » Initial oral dose 4mg/5mg x Once daily
 - » Dosage range: 4mg/5mg upto 8mg/10mg x Once daily
- ✎ OR Tab. Losartan + Hydrochlorothiazide 50mg/12.5mg or 100mg/25mg (Co-Eziday)
 - » Initial oral dose 50mg/12.5mg x Once daily
 - » Dosage range: 50mg/12.5mg upto 100mg/25mg x Once daily
- ✎ OR Valsartan + Hydrochlorothiazide 80mg/12.5 or 160mg/12.5mg or 160mg/25mg (Co-Diovan)
 - » Initial oral dose 80mg/12.5mg x Once daily
 - » Dosage range: 80/12.5mg upto 160mg/25mg x Once daily (OD)



If not controlled with COMBINE TWO DRUGS (ACEI or ARB + CCB), add Diuretics

1. Lifestyle modifications for managing hypertension (as mentioned above)

2. Choice of Anti-Hypertensive Agent

- ✎ Tab. Amlodipine 5mg + Valsartan 160mg + Hydrochlorothiazide 12.5mg (5/160/12.5mg)
 - » Initial oral dose Tab. Exforge HCT 5/160/12.5mg x Once daily
 - » Dosage range: 5/160/12.5mg upto 10/320/25mg x Once daily
 - » Other available brand in Pakistan
 - ✎ Tab. Avsar Plus
 - ✎ Tab. Co-Extor
 - ✎ Tab. Sofvasc-HCT
- ✎ OR Tab. Olmesartan 20mg + Amlodipine 5mg + Hydrochlorothiazide 12.5mg (Co-Olesta-AM)
 - » Initial oral dose Tab. Co-Olesta AM 20/5/12.5mg x Once daily
 - » Dosage range: 20/5/12.5mg upto 40/10/25mg x Once daily
- ✎ OR Tab. Perindopril 5mg + Indapamide 1.25mg + Amlodipine 5mg (Triplixam 5/1.25/5mg)
 - » Initial oral dose Tab. Co-Olesta AM 20/5/12.5mg x Once daily
 - » Dosage range: 20/5/12.5mg upto 40/10/25mg x Once daily

Available strength in all brands
 Tab Exforge-HCT 5/160/12.5mg
 Tab Exforge-HCT 10/160/12.5mg
 Tab Exforge-HCT 5/160/25mg
 Tab Exforge-HCT 10/160/25mg
 Tab Exforge-HCT 10/320/25mg

Available strength
 Tab Co-Olesta AM 20/5/12.5mg
 Tab Co-Olesta AM 40/5/25mg
 Tab Co-Olesta AM 40/10/25mg

Available strength
 Tab Triplixam 5/1.25/5mg
 Tab Triplixam 5/1.25/10mg
 Tab Triplixam 10/2.5/5mg
 Tab Triplixam 10/2.5/10mg

For Resistant hypertension

Uncontrolled Hypertension with three classes of anti-hypertensive drugs and the drug should include diuretics

For example: PATIENT ON ACEI/ARB + CCB + THIAZIDES DIURETICS (Hydrochlorothiazide, Indapamide) and BP still not controlled then ADD, ONE of the following medications: ALPHA-BLOCKER OR VASODILATING BETA-BLOCKER.

- ✎ Alpha-blocker: Prazosin, Terazosin, and Doxazosin
- ✎ OR Vasodilating beta-blocker: Nebivolol, Carvedilol



ANTI-HYPERTENSIVE TREATMENT BASED ON COMORBIDITIES

Comorbidity	Treatment Recommendations
History of stroke or Transient Ischaemic attacks (TIA)	Initial therapy » Monotherapy: Thiazides, ACEIs, or ARBs » Combination therapy: Thiazides PLUS either ACEIs or ARBs Treatment goal: Blood pressure < 130/80mmHg in most patients
Ischemic Stroke (systolic BP >180–200 mmHg)	Recommended drugs: Labetolol, Nicardipine Drug to avoid: Nitroprusside, methyldopa, clonidine, nitroglycerin
Intracerebral hemorrhage (systolic BP >140–160 mmHg)	Recommended drugs: Labetolol, Nicardipine Subarachnoid hemorrhage: Should give nimodipine for 3 weeks following presentation to minimize cerebral vasospasm. Drug to avoid: Nitroprusside, Methyldopa, Clonidine, Nitroglycerin
Stable Ischemic Heart Disease	Initial therapy: ACEIs or ARBs PLUS Beta blockers, as indicated for pharmacotherapy for coronary artery disease (CAD) Add-on therapy » For patients with angina: Dihydropyridine CCBs » For patients without angina: Dihydropyridine CCBs, Thiazides, OR Aldosterone antagonists Treatment goal: Blood pressure <130/80mmHg
Acute Kidney Injury	Recommended drugs: Fenoldopam, Nicardipine, Clevidipine
Chronic Kidney Disease (CKD)	Initial therapy » For patients with microalbuminuria and diabetes, or with overt proteinuria: ACEIs or ARBs » For patients with microalbuminuria but no diabetes: Consider ACEIs or ARBs Treatment goal: SBP <120mmHg (if tolerated)
Diabetes mellitus	Initial therapy » For patients with microalbuminuria or overt proteinuria: ACEIs or ARBs (Protective against diabetic nephropathy) » For patients without albuminuria: any first-line agent (ACEIs, ARBs, CCBs, OR Thiazide diuretics) Treatment goal: Blood pressure < 130/80mmHg
Congestive Heart Failure (CHF)	Initial therapy » Heart failure with reduced ejection fraction (HFrEF): Guideline-Directed Medical Therapy ▪ Beta Blockers (Carvedilol, or Metoprolol succinate, or Bisoprolol) – Recommended for use in compensated CHF. – Must be used cautiously in decompensated CHF. – Contraindicated in cardiogenic shock. ▪ Diuretics, including aldosterone antagonists. ▪ ACEIs or ARBs ▪ Angiotensin receptor-neprilysin inhibitor » Heart failure with preserved ejection fraction (HFpEF) ▪ Current volume overload: Diuretics ▪ No current volume overload: ACEIs or ARBs PLUS Beta Blockers ▪ AVOID NITRATES. Treatment goals » HFrEF: Blood pressure <130/80 mmHg » HFpEF: Systolic BP < 130 mmHg
Asthma	Initial therapy: ARBs, CCB, OR thiazide diuretics (no preference) Cautions » Avoid Beta Blockers unless for a particular indication. » Use cardio-selective beta blockers when necessary (non-cardio-selective beta blockers can cause bronchoconstriction). » ARBs may be preferred over ACEIs (increased risk of cough)
Osteoporosis	Initial therapy: thiazide diuretics (↓ renal calcium excretion → ↓ bone loss)
Gout	Initial therapy » ARBs (e.g., Losartan, have an uricosuric effect), ACEIs, and CCBs » Thiazide diuretics should be avoided (↑ uric acid levels).
Preeclampsia, Eclampsia	Initial therapy » Labetolol

HYPERTENSION LONG-TERM MANAGEMENT AND FOLLOW-UP

GENERAL PRINCIPLES

- Goals include evaluating medication adherence, monitoring treatment and relevant laboratory studies, and adjusting medication.
 - » Patients on non-pharmacological treatment alone: Follow up after 3–6 months.
 - If blood pressure is uncontrolled: Initiate pharmacological treatment.
 - » Most patients initiated pharmacological treatment: Follow up after = 1 month.
 - If blood pressure is uncontrolled: Continue to escalate therapy at one-month intervals.
 - Once blood pressure is controlled: Reassess after 3–6 months and annually thereafter if blood pressure remains stable.

LABORATORY MONITORING

- Serum electrolytes
 - » For most patients, check at the one-month follow-up visit.
 - » Checking after = 2 weeks may be reasonable in certain patients, e.g.:
 - Patients with initial low serum sodium who were started on a thiazide diuretic.
 - Patients with chronic kidney disease (CKD) and initial high creatinine or high normal potassium who were started on an ACEI or ARB.
- Serum creatinine
 - » Check within 2–4 weeks in patients with CKD who were started on an ACEI or ARB.
 - » Discontinuation of ACEIs or ARBs is usually not necessary if creatinine increases by < 30% from baseline without concomitant hyperkalemia or fluid retention.

MEDICATION TITRATION

- Adjust medication based on adverse effects, e.g.:
 - » Hyponatremia: Discontinue or avoid thiazide diuretics; consider loop diuretics if necessary.
 - » Hypokalemia: Consider initiating a potassium-sparing diuretic after ruling out hyperaldosteronism.
 - » Hyperkalemia: Consider restricting dietary potassium or initiating a thiazide diuretic or cation-exchange polymer after ruling out pseudohyperkalemia.
 - » Cough in patients on ACEIs: Switch to an ARB.
- Adjust medication to reach optimal blood pressure control.
 - » Reassess within 4 weeks of initiating or changing pharmacological therapy.
 - » Ask about medication adherence.
 - » If indicated, adjust medications using one of the following strategies:
 - Increasing the dose of the initial drug
 - Switching to another drug ("sequential monotherapy")
 - Adding a second drug (in the form of a single combination pill, if possible)
 - » If the treatment goal cannot be reached with two drugs:
 - Add a third drug.
 - Evaluate for secondary causes of hypertension, if indicated.
- If blood pressure is controlled: Reassess after 3–6 months and annually thereafter.



ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION (STEMI)

- Definition: Myocardial infarction is the irreversible necrosis of heart muscle (acute myocardial injury) that occurs because of a prolonged mismatch between perfusion and demand due to occlusion in the coronary arteries.
- Risk factors: Cigarette smoking, Hypertension, Diabetes mellitus, abdominal obesity, Metabolic syndrome, Physical inactivity, blood lipid abnormalities, Renal dysfunction, Positive family history (the younger the onset in a first-degree relative, the greater the risk of premature angina, MI, angioplasty, or bypass surgery, Advanced age, Male sex, cocaine use, psychosocial factors, and consumption of too few fruits and vegetables and too much alcohol.
- Metabolic syndrome is defined as a constellation of three or more of the following: abdominal obesity, triglycerides ≥ 150 mg/dL, HDL cholesterol < 40 mg/dL for men or < 50 mg/dL for women, fasting glucose ≥ 110 mg/dL, and HTN.

CLASSIFICATION – MYOCARDIAL INFARCTION (MI) IS CLASSIFIED INTO 5 SUBTYPES

- Type-1 MI:** MI caused by atherosclerotic plaque disruption or acute coronary thrombosis. Most common form.
- Type-2 MI:** MI secondary to an oxygen supply/demand mismatch. Less common form (14%).
- Type-3 MI:** MI resulting in death when cardiac enzymes values (biomarkers) are not available.
- Type-4 myocardial infarction (MI):** MI related to percutaneous coronary intervention.
 - Type 4a: MI ≤ 48 hours after PCI (Percutaneous coronary intervention).
 - Type 4b: MI related to stent thrombosis.
 - Type 4c: MI associated with restenosis after PCI.
- Type-5 myocardial infarction (MI):** MI related to coronary artery bypass grafting.

CLINICAL FEATURES

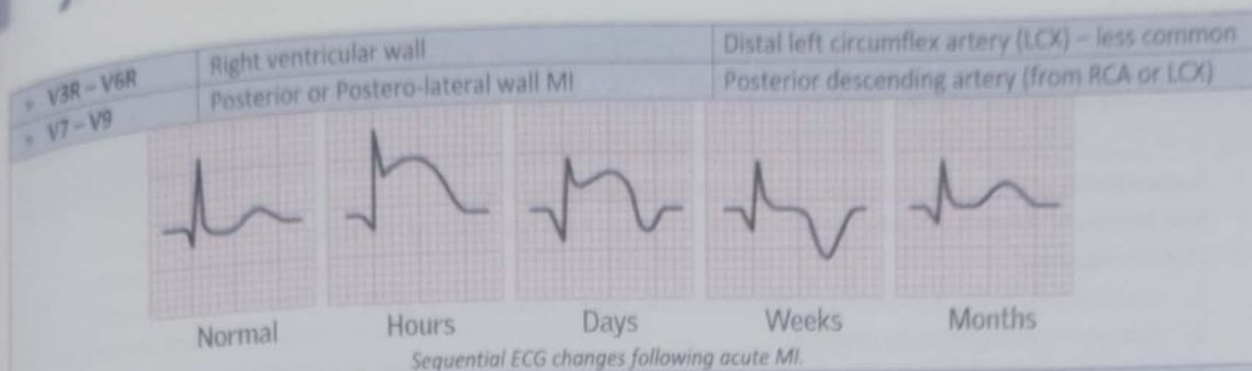
- Chest pain: Acute retrosternal chest pain, dull and squeezing, radiating to radiating to left chest, arm, shoulder, neck, jaw, and/or epigastrium, often, worsened by exertion, stress, not relieved by nitrates, often peaking in the morning.
- Dyspnea, pallor, nausea, vomiting, diaphoresis, dizziness, and anxiety/Distress (sense of doom or death)
- Additional features:
 - Tachycardia, arrhythmias, symptoms of CHF (orthopnea, pulmonary edema, or cardiogenic shock), murmur
 - Atypical presentations (more common in elderly, diabetic individuals, and women): Stabbing, sharp chest pain, minimal or absent chest pain ("Silent MI"), autonomic symptoms like nausea and diaphoresis.
 - Features more commonly seen in inferior wall MI: Epigastric pain, bradycardia, and clinical TRIAD of right ventricular infarction such as 1. Hypotension, 2. Elevated jugular venous pressure (JVP), 3. Clear lung fields.

DIAGNOSTIC WORKUP

- Best early test: 12-LEADS ECG $\rightarrow$ ST-segment elevation of at least 1 mm in 2 or more contiguous leads.
- Cardiac biomarkers: (TROP-I > TROP-T) at 2 hours, then every 8 hours for 3 days, Myoglobin $\uparrow$ in first hour.
 - Serum Troponin: Elevated levels are highly sensitive and specific for myocardial injury.
 - Total CK-MB: Elevated CK-MB levels indicate myocardial injury.
 - LDH: Elevation may occur 24-48 hours after MI onset, peaking at 3-4 days due to cell necrosis.
- Serum electrolytes: May be normal (Sodium &/or potassium – which may be affected during acute MI).
- Inflammatory marker: Serum CRP elevated.
- Blood glucose: normal or $\uparrow$ (Hyperglycemia is commonly seen in acute MI, with or without a history of DM).
- Lipid profile (12 hours fasting)
- CBC: Elevated WBCs count may indicate inflammation associated with MI. May show anemia.
- Liver function tests: deranged, AST level may be elevated due to cell injury/necrosis.
- Chest X-ray: often normal, used to exclude possible alternative diagnosis of chest pain (e.g. pulmonary edema)
- Coronary Angiography: Definitive test of choice to confirm for diagnosis of thrombus with occlusion of the artery to identify site and degree of vessel occlusion. Coronary angiography carried out as early as possible, with target first medical contact-to-device time < 90 min in patients with STEMI to facilitate early reperfusion and save myocardium.
- Echocardiography: Indicated for all patients with acute myocardial infarction (MI) after reperfusion therapy, to assess left ventricular function. Useful for further risk stratification in patients with an atypical presentation

LOCATION OF MYOCARDIAL INFARCT BY ECG LEADS

ECG leads affected	Infarct location wall of the heart	Vessel involvement
V1 – V6	Extensive anterior (aVL, I may also be affected)	Left anterior descending artery (LAD)
V1 – V2	Antero-septal wall MI	Left anterior descending artery (LAD)
V3 – V4	Antero-apical wall MI	Left anterior descending artery (LAD)
V5 – V6	Antero-lateral wall MI	Left anterior descending artery (LAD)
I, aVL, V5 & V6	Lateral wall MI	LAD & left circumflex artery (LCX)
II, III, & aVF	Inferior wall MI	Proximal Left circumflex artery (LCX)
		Right coronary artery (RCA) – more common



PREVENTION OF MYOCARDIAL INFARCTION/STEMI FOR ACUTE TREATMENT OF MI/STEMI – SEE EMERGENCY SECTION

Modify risk factors

- » Patients should be strongly advised, and helped, to stop smoking.
- » Identify and treatment of diabetes mellitus, hypertension, hyperlipidaemia, and CKD.
- » Advise a diet high in oily fish, fruit, vegetables, & fibre, and low in saturated fats.
- » Encourage daily exercise. Refer to a cardiac rehab programme.
- » Mental health: flag to the patient's general practitioner (GP) if depression or anxiety are present—these are independently associated with poor cardiovascular outcomes.

DUAL ANTIPLATELET THERAPY (DAPT) to ↓ vascular events (e.g. MI, stroke).

- » Lifelong Low-dose aspirin: Tab. Aspirin 75mg (Loprin, Ascard) x once daily, once daily (OD)
- » AND add one of the following: for at least 12 months
 - ↳ Tab. Prasugrel 10mg (Eficlot, Obsoprel) at loading dose 60mg, PO, once on DAY1, then 10mg x OD.
 - ↳ OR Tab. Ticagrelor 90mg (Brilinta, Anplag) at loading dose 180mg, PO, once on DAY1, then 90mg x BD.
- (Both above drugs demonstrated superior outcomes to clopidogrel in clinical studies of primary PCI).
- ↳ OR Tab. Clopidogrel 75mg (Lowplat) x loading dose 300 to 600mg, then 75mg once daily

High dose Statins: Early initiation of high-intensity statin regardless of baseline cholesterol, LDL, and HDL levels.

- » Tab. Atorvastatin 40mg (Lipitor, Lipiget) x Once daily. **Dosage:** ≥ 40mg (upto 80mg/day)
- » OR Tab. Rosuvastatin 20mg (X-Plended, Rovista) x Once daily. **Dosage:** ≥ 20mg (up to 40mg/day)

Consider cardioprotective drugs as indicated:

1. **Beta Blockers:** reduces myocardial oxygen demand, (avoid in patients with hypotension, asthma, features of heart failure, and/or risk of cardiogenic shock). **Start low and increase slowly, monitoring pulse and BP.** Hold if systolic BP <100 mmHg, Heart rate <50 beat/minute.

- » Tab. Carvedilol 6.25mg (Carveda, Carlov) x started at a dose of 6.25mg orally twice daily and may be increased 12.5mg, and then 25mg BD. **Available strength:** 3.125mg, 6.25mg, 12.5mg and 25mg
- » OR Tab. Metoprolol 25mg OR 50mg (Merol) x Tartrate initially 12.5mg orally every 6 hours, increase to 25 to 50mg every 6 hours as tolerated) in eligible patients, beginning within the 1st 24hr.

2. **ACE inhibitors (or ARB) in all patients. Monitor renal function.**

- » Consider in patients if any of the following are present:

- 1) ST segment elevation MI (STEMI) – especially in those patient with ECG finding of anterior MI.
- 2) Left ventricular EF ≤40%
- 3) Patient with Hypertension
- 4) Patient with Heart failure
- 5) Patient with Diabetes mellitus

- » Tab. Lisinopril 5mg or 10mg (Zestril, Trupril) 2.5mg up to 5mg x OD titrated at target dose 10mg x OD

- » OR ARBs, if contraindication to ACEIs (Dry cough, angioedema): Tab. Valsartan 160mg (Exforge, Diovan) x Twice daily (BD) is equivalent to captopril in reducing mortality.

3. Do an echo to assess LV ejection fraction (LVEF). Add aldosterone antagonist (eg spironolactone) if LVEF <40%.

Gastroprotective: Tab. Pantoprazole 40mg (Zopent) x per orally x once daily (OD)

Stool softener: Syp. Lactulose (Duphalac) 30ml x HS or Skilax drops up to 10 – 20 drops in a half cup water x OD/BD

Anxiolytic or hypnotic if needed: Alprazolam 0.5mg, lorazepam 1-2mg, or diazepam 5-10mg x HS as needed

Reperfusion Therapy: Percutaneous coronary intervention (PCI) preferable over Fibrinolytic therapy → Primary PCI with stenting is the treatment of choice, should be done, if available within 90 minutes and if primary PCI is unavailable within <120 minutes → Fibrinolytic therapy. See MI/STEMI Emergency section for detail.

Revascularization: All patients with suspected acute coronary syndrome (ACS) should be considered for emergency percutaneous coronary intervention (PCI). Patients with multivessel disease may be considered for CABG instead of PCI. Consider dual antiplatelet therapy after PCI with stent placement for at least 12 months.

STABLE ANGINA PECTORIS

Clinical features

- ☞ Cause: Stable atheroma (collection of lipids covered by fibrous cap).
- ☞ Risk factors of Atherosclerosis: Hypertension, Diabetes mellitus, Obesity, Smoking.
- ☞ Clinical features:
 1. Constricting/heavy discomfort to the chest, jaw, neck, shoulders, or arms.
 2. Symptoms brought on by exertion.
 3. Symptoms relieved within 5 minutes by rest or glyceryl trinitrate (GTN).
- ☞ Criteria: All 3 features = typical angina; 2 features = atypical angina; 0-1 features = nonanginal chest pain.
- ☞ Other precipitants: emotion, cold weather, and heavy meals.
- ☞ Associated symptoms: dyspnoea, nausea, sweatiness, faintness. **Features that make angina less likely:** pain that is continuous, pleuritic, or worse with swallowing; pain associated with palpitations, dizziness or tingling.

Diagnostic workup

- ☞ ECG at rest – Normal. **Exercise tolerance test (ETT) or Exercise ECG** to assess for ischaemic ECG changes by using a standard treadmill or bicycle ergometer protocol
- ☞ Cardiac Enzyme: Normal
- ☞ Functional imaging: myocardial perfusion scintigraphy, stress echocardiography (echo whilst undergoing exercise or receiving dobutamine), cardiac MRI
- ☞ CT coronary angiography is the imaging investigation of first choice.
- ☞ Chest X-ray: normal, look for cardiomegaly, pulmonary oedema, or a widened mediastinum.
- ☞ Consider other investigation: CBC, HbA1C, Serum creatinine, Lipid profile (12 hour fasting)



First line Prescription #1

☞ Acute Attacks of Angina:

- ☞ **Short acting Nitrates:** Glyceryl trinitrate (GTN) – Tab. Angised 0.5mg x sublingually (SL) OR Nitrl 0.4mg spray Translingual (apply the drug to the top of the tongue), provide immediate relief of effort angina. Advise the patient to repeat the dose if the pain has not relieved after 5 minutes and to call an ambulance if the pain is still present 5 minutes after the second dose

☞ All patients should be educated on risk factor reduction

1. Lifestyle recommendations: Smoking cessation, recommended physical activity, a healthy diet, and maintaining a healthy weight
 2. Start prevention of recurrent coronary artery disease (CAD): antiplatelet agents, statins, and management of comorbidities (diabetes mellitus, hypertension, CKD)
- ☞ Initiate Anti-anginal drugs: First line – betablockers, second line – CCBs and nitrates, third line – Renalazine
1. First line treatment with Beta-Blockers (All beta-blockers are equally effective)
 - » Tab. Bisoprolol 5mg (Concor) start at dose 2.5mg than titrated up to 5mg, if not controlled than 10 mg x OD (Max: 20mg/day)
 - » OR Tab. Carvedilol (Carvida, Carlov, Dilatrend) start at a dose of 3.125mg orally BD and may be increased to 6.25mg than 12.5mg, and max 25mg twice daily at intervals of approximately 2 weeks.
 - » OR Tab. Metoprolol 25mg, 50mg (Merol) x start at dose 25mg x BD than 50mg titrated up 100mg x BD (Max 400mg/day)
 - ☞ **If serious contraindication to Beta-Blockers → second line drugs (CCBs) OR Nitrates – prescription #2**
 2. Start prevention of recurrent coronary artery disease (CAD): Medications that decrease morbidity and mortality
 3. Anti-Platelet: Tab. Aspirin 75mg (Loprin, Ascard) x at dose 75mg up to 150mg x OD (Patients who cannot tolerate aspirin or have aspirin insensitivity or serious adverse effects → Clopidogrel)
 - ☞ Tab. Clopidogrel 75mg (Lowplat, Clopid, Nociot) x OD
 4. High dose statin therapy: Current U.S. guidelines recommend high-dose statin therapy (Atorvastatin up to 80 mg per day or rosuvastatin up to 40 mg per day) without monitoring of LDL levels.
 - » Tab. Atorvastatin 40mg (Lipitor, Lipiger) started at dose 40mg upto 80mg/day x OD
 - » OR Tab. Rosuvastatin 20mg (X-Plended, Rovista) started at dose 20mg up to 40mg/day x OD

5. Consider ACEIs or ARBs in patients with Hypertension, Diabetes mellitus, Left ventricular EF ≤ 40% and CKD
 - » ACEIs: Tab. Ramipril 5mg OR 10mg x start at 2.5mg than titrated to 5mg once daily (OD); titrate up 10mg x OD
 - » OR ARBs: Tab. Losartan 25mg OR 50mg x Start at dose 25mg titrated up to 100mg x per orally, once daily (OD)

Prescription #2 (second line treatment)

Rx
Acute Attacks of Angina:

- Short acting Nitrates: Glyceryl trinitrate (GTN) – Tab. Angised 0.5mg x sublingually (SL) OR Nitro 0.4mg spray x Translingual (apply the drug to the top of the tongue), provide immediate relief of effort angina. Advise the patient to repeat the dose if the pain has not relieved after 5 minutes and to call an ambulance if the pain is still present 5 minutes after the second dose
- All patients should be educated on risk factor reduction
- Lifestyle recommendations: Smoking cessation, recommended physical activity, a healthy diet, and weight
- Start prevention of recurrent coronary artery disease (CAD): antiplatelet agents, statins, and management of comorbidities (diabetes mellitus, hypertension, CKD)

1. Antianginal

Second line: Calcium channel blockers (CCBs):

- Tab. Verapamil 80mg (Calan, Isoptin) x three times daily (TDS) or verapamil sustained released tablets (Calan SR, Isoptin SR) 240mg x once daily (OD)
- Dosage: 80mg to 160mg x TDS or Sustained-Release (SR) tablet 240mg to 480mg/day
- OR Tab. Diltiazem 30mg or 60mg (Dilzem, Herbesser) at dose 30mg x TDS (if not controlled 60mg x TDS)
- OR Tab. Amlodipine 5mg or 10mg (Norvasc, Sofvasc) x started at 2.5mg then titrated 5mg up to 10mg x OD

If not controlled with CCBs → replace and consider Long-acting nitrates:

- Tab. Isosorbide mononitrate 20mg (Monis, Elanatan) x 10mg upto 40mg x twice daily (BD)
- OR Tab. Monis SR 60mg x started at dose 60mg to 120mg x once daily (OD)
- OR Tab. Isosorbide dinitrate 10mg (Isoket, Isdin) x 1-2 tab. x TDS. Dosage: 10 to 40mg x TDS

Third line drug: Consider Renolazine if beta-blockers, CCBs, and nitrates are ineffective or not tolerated.

- Tab. Renolazine 500mg (Rancard XR, Angiwell XR) x Started at a dose of 500mg twice daily and titrated up to a maximal dose of 1000 mg twice daily. Side-effects: Q.T prolongation, should be avoided with those who are taking drugs which causes Q.T prolongation.
- Tab. Ivabradine 5mg (Coralan, Ivadin): reduces heart rate with minimal impact on BP. Patient must be in sinus rhythm. Start with 5mg twice daily (BD). Only consider if clinical heart failure also present.
- Tab. Nicorandil 10mg (Nicoril, Nicoget): Potassium channel activator. Start with 5–10mg x Twice daily (BD).
- Contraindications: acute pulmonary edema, severe hypotension, hypovolaemia, LV failure.

2. Start prevention of recurrent coronary artery disease (CAD): Medications that decrease morbidity and mortality

- Anti-Platelet: Tab. Aspirin 75mg (Loprin, Ascard) x at dose 75mg up to 150mg x OD (Patients who cannot tolerate aspirin or have aspirin insensitivity or serious adverse effects → Clopidogrel).
- Tab. Clopidogrel 75mg (Lowplat, Clopid, Noclote) x OD
- High dose statin therapy: Current U.S. guidelines recommend high-dose statin therapy (Atorvastatin up to 80 mg per day or rosuvastatin up to 40mg/day) without monitoring of LDL levels.
- Tab. Atorvastatin 40mg (Lipitor, Lipiget) started at dose 40mg upto 80mg/day x OD
- OR Tab. Rosuvastatin 20mg (X-Plended, Rovista) started at dose 20mg up to 40mg/day x OD
- Consider ACEIs or ARBs in patients with Hypertension, Diabetes mellitus, Left ventricular EF ≤ 40% and CKD
- ACEIs: Tab. Ramipril 5mg OR 10mg x start at 2.5mg then titrated to 5mg once daily; titrate up 10mg x OD
- OR ARBs: Tab. Losartan 25mg OR 50mg x Start at dose 25mg titrated up to 100mg x per orally x (OD)

Select patients: Revascularization → Percutaneous coronary intervention with coronary stenting OR Coronary artery bypass grafting (CABG).

Revascularization is harmful in patients who do not meet anatomical or physiological criteria for intervention.

Canadian Cardiovascular Society (CCS) Grading of Angina Pectoris	
Grade	Description
Grade I	Ordinary physical activity does not cause angina, such as walking and climbing stairs. Angina with strenuous or rapid or prolonged exertion at work or recreation
Grade II	Slight limitation of ordinary activity. Walking or climbing stairs rapidly, walking uphill, walking or stair climbing after meals, or in cold, or in wind, or under emotional stress, or only during the few hours after awakening. Walking more than two blocks on the level and climbing more than one flight of ordinary stairs at a normal pace and in normal conditions
Grade III	Marked limitation of ordinary physical activity. Walking one or two blocks on the level and climbing one flight of stairs in normal conditions and at normal pace
Grade IV	Inability to carry on any physical activity without discomfort, anginal syndrome may be present at rest

UN-STABLE ANGINA/NSTEMI

- ☞ **Cause:** Unstable angina is due to un-stable atheroma (MI in evolution-Partial occlusion of coronary vessel). NSTEMI is classically due to partial occlusion of a coronary artery → affects the inner layer of the heart (subendocardial infarction)
- ☞ **Risk factor of Atherosclerosis:** Hypertension, Diabetes, Obesity, Smoking, Hyperlipidemia, Family history of IHD
- ☞ **Clinical features**
 - » **Retrosternal Chest Pain:** chest pain describes as pressure squeezing, burning or tightness/heaviness. Pain may radiate to left shoulder and arm, neck, jaw and back. Not relieved by rest or nitrates.
 - » **Other symptoms:** Levine's sign (Clenched fist held over the chest), Dyspnea, Dizziness, Palpitations, Restlessness, Anxiety and Autonomic symptoms such as Diaphoresis, nausea, vomiting, syncope.
 - » **Three principle presentation:**
 1. Rest angina >20 minutes in last week
 2. New onset angina in last 2 months
 3. Increasing angina: increased frequency, duration, or severity.

Diagnostic workup

- ☞ **ECG:** No ST elevations, normal or show ST depression, loss of R wave, T-wave inversion
- ☞ **Exercise tolerance test (ETT) or Exercise ECG:** using a standard treadmill or bicycle ergometer protocol
- ☞ **Cardiac enzyme:** Normal in Un-stable angina, Elevated in NSTEMI within 1–6 hours
- ☞ **Stress echo:** Echo whilst undergoing exercise or receiving dobutamine
- ☞ **CT coronary angiography** is the imaging investigation of first choice.
- ☞ **Chest X-ray:** normal, Look for cardiomegaly, pulmonary oedema, or a widened mediastinum.
- ☞ **Consider other investigation:** CBC, HBA1C, Serum creatinine, Lipid profile (12 hour fasting)



Treatment See MI/STEMI (mentioned above and emergency section for acute treatment)

- ☞ Stabilize patients using ABCD&E approach.
- ☞ Invasive management depends on risk stratification such as TIMI score.
- ☞ The standard protocol for ACS typically involves a combination of interventions including:
 1. Immediate assessment of symptoms and risk factors.
 2. Administration of oxygen: Give in patient with cyanosis or hypoxemia (<94 SpO₂) → Nasal O₂ at 2 L/min.
 3. **DUAL ANTIPLATELET THERAPY (DAPT)** to ↓ vascular events (e.g. MI, stroke).
 - » **Tab. Aspirin 300mg** (Disprin) one tablet per oral once (PO) or **Tab. Aspirin 75mg** (Loprin, Ascard) 4 tablets PO, once followed by **Tab. Aspirin 75mg** or 150mg at dose 75 – 150 mg once daily.
 - » **AND add one of the following:**
 - ☞ **Tab. Prasugrel 10mg** (Eficlot, Obsoprel) at loading dose 60mg, PO, once on DAY1, then 10mg x OD.
 - ☞ **OR Tab. Ticagrelor 90mg** (Brilinta, Anplag) at loading dose 180mg, PO, once on DAY1, then 90mg x BD.
 - (Both above drugs demonstrated superior outcomes to clopidogrel in clinical studies of primary PCI).
 - ☞ **OR Tab. Clopidogrel 75mg** (Lowplat) x loading dose 300 to 600mg, then 75mg once daily
 4. **Anticoagulate with Inj. Enoxaparin** at dose 1mg/kg BD (OD if GFR <30mL/min), **OR Inj. Heparin** at dose 60 units/kg (max 4000 Units), IV bolus initially, followed by 12 units/kg/hour infusion (max of 1000 units), adjust dose to target aPTT 1.5–2.0 x control (about 50–70 seconds), until discharge
 5. **Nitrates:** Provide rapid relief to pain if chest pain persists. Do not use if Systolic BP is < 90 mm Hg.
 - » **Glyceryl Trinitrate 0.4mg/dose** (Nitrl spray) 1 spray SL (Sublingually)
 - » **OR Tab. Glyceryl Trinitrate 0.5mg** (Angised) x 1 tablet SL (Sublingually)
 6. **Analgesia for pain management:** **Inj. Morphine sulphate 10mg/ml** x at dose of 4–8mg or **Inj. Nalbuphine 20mg/ml** (Kinz) at dose 10 to 20 mg, diluted in 0.9% NS x IV. Subsequent small doses can be given every 15 minutes until adequate pain control is achieved. Monitor patients for signs of respiratory depression. **Adjunct antiemetic therapy** is recommended in combination with morphine or Nalbuphine to manage potential nausea and vomiting associated with opioid administration such as **Inj. Metoclopramide 10mg/2ml** (Metaclo) or **Inj. Dimenhydrinate 50mg/1ml** (Gravinate) x IV.
 7. **Continuous cardiac monitoring:** Cardiac monitor, Serial ECG and Serial troponin levels.
 - » **High dose Statins:** Early initiation of high-intensity statin regardless of baseline cholesterol, LDL, and HDL levels.
 - » **Tab. Atorvastatin 40mg** (Lipitor, Lipiget) x Once daily (OD). **Dosage:** ≥ 40mg (upto 80mg/day)
 - » **OR Tab. Rosuvastatin 20mg** (X-Plended, Rovista) x Once daily (OD). **Dosage:** ≥ 20mg (up to 40mg/day)
 - » **Consider cardioprotective drugs as indicated:** Beta Blockers, ACE inhibitors (or ARB), Aldosterone antagonist
 - » **Glycoprotein IIb/IIIa inhibitor (GPI)** → Consider in intermediate/high-risk patients with early-invasive strategy → **Inj. Tirofiban 12.5mg/50ml** (AGGRASTAT) x IV x at dose of 25mcg/kg within 5 min and then 0.15 mcg/kg/min for up to 18hrs.

CONGESTIVE CARDIAC FAILURE (CHF)

RISK FACTORS & CAUSES OF HEART FAILURE

Risk factors

- » Coronary Artery Disease
- » Viral Infection
- » Alcohol Abuse
- » Hypertension
- » Arrhythmias
- » Metabolic Syndrome
- » Drugs: Doxorubicin
- » Smoking

Causes of Systolic Dysfunction (Reduced EF)

- » Ischemic Heart Disease (most common)
- » Chronic Hypertension
- » Valvular heart Disease
- » Congenital Heart Disease
- » Dilated cardiomyopathy: Chagas disease, chronic alcohol use, idiopathic
- » Cardiac arrhythmias
- » Myocarditis

Causes of Diastolic Dysfunction (Preserved EF)

- » Hypertension with left ventricular hypertrophy
- » Hypertrophic cardiomyopathy
- » Amyloidosis
- » Sarcoidosis
- » Hemochromatosis
- » Scleroderma
- » Post-operative/radiation fibrosis

High-Output Heart Failure

- » Obesity
- » Myeloproliferative Disorder
- » Arterial-Venous Fistula
- » Hyperthyroidism/Thyrotoxicosis
- » Severe anemia
- » Pregnancy
- » Beri-beri

STAGES AND CLASSIFICATION OF HEART FAILURE

NYHA functional classification

The NYHA (New York Heart Association) functional classification system is used to assess the patient's functional capacities (i.e., limitations of physical activity and symptoms) and has prognostic value.

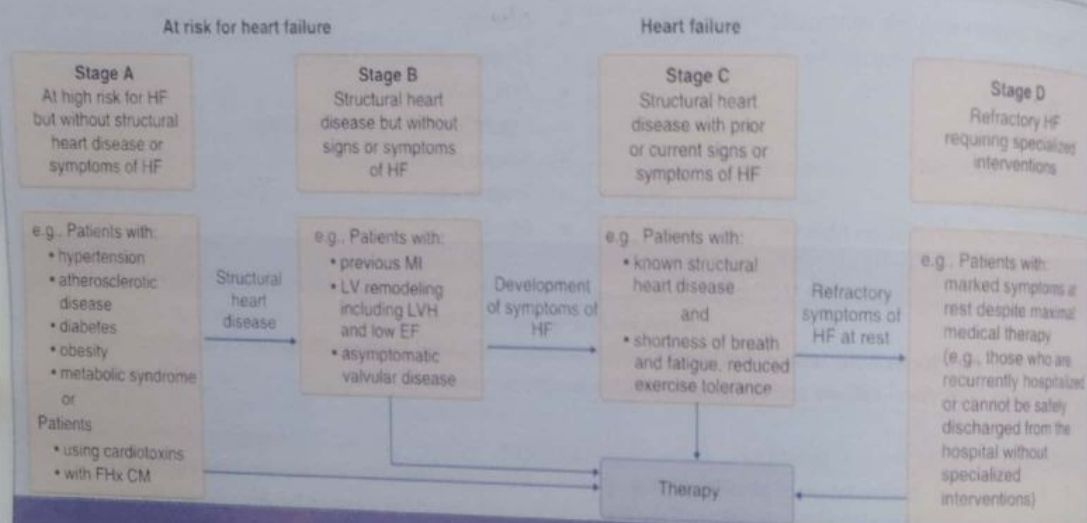
NYHA Class	Definition	Limitation	Example
I	» No limitation of physical activity. » Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea (shortness of breath).	None	Can complete any activity requiring ≤ 7 MET: » Carry 11 kg up 8 steps » Carry objects weighing 36 kg » Shovel snow » Spade soil » Ski » Play squash, handball, or basketball » Jog or walk 8 km/hour
II	» Slight limitation of physical activity. Comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea (shortness of breath).	Mild	Can complete any activity requiring ≤ 5 MET: » Sexual intercourse without stopping » Garden » Roller skate » Walk 7 km/hour on level ground » Climb one flight of stairs at a normal pace without symptoms
III	» Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation, or dyspnea.	Moderate	Can complete any activity requiring ≤ 2 MET: » Shower or dress without stopping » Strip and make a bed » Clean windows » Play golf » Walk 4 km/hour
IV	» Unable to carry on any physical activity without discomfort. Symptoms of heart failure at rest. If any physical activity is undertaken, discomfort increases.	Severe	Cannot do or cannot complete any activity requiring ≥ 2 MET; cannot do any of the above activities

MET = metabolic equivalent of task, a measure of how much energy is expended compared to remaining at rest.

American Heart Association (AHA) classification (2013)

The AHA classification system categorizes patients according to the stage of disease based on an objective assessment of clinical features and diagnostic findings.

Stage	Objective assessment	Corresponding NYHA functional class
Stage A	» High risk of developing heart failure (e.g., preexisting arterial hypertension, coronary artery disease, diabetes mellitus) » No structural cardiac changes or symptoms	No corresponding NYHA class
Stage B	» Structural damage to the heart (e.g., infarct scars, dilatation, hypertrophy) » No signs or symptoms of heart failure	NYHA I
Stage C	» Structural heart disease with prior or current signs or symptoms of Heart Failure	NYHA I, II, III, IV
Stage D	» Terminal stage heart failure (Refractory HF) requiring specialized interventions	NYHA IV



CLINICAL FEATURES OF CONGESTIVE HEART FAILURE (CHF)

General features of heart failure

- » Nocturia, Fatigue, Dizziness and faintness
- » Palpitation, Tachycardia, various arrhythmias
- » **Auscultation:** S3/S4 gallop on auscultation
- » **Pulsus alternans:** A physical finding characterized by alternating one strong beat and one weak beat (with a regular pulse rhythm) caused by alterations in cardiac output. Associated with heart failure and cardiac tamponade.
- » **Cardiac Cachexia:** Unintentional severe weight loss caused by severe heart failure.

Clinical features of Right-sided heart failure (RHF)

N.B. Isolated Right sided heart failure (RHF) is very rare, if occurs so due to lung pathologies

Symptoms of fluid retention and increased CVP

- » **Peripheral pitting edema:** as a result of fluid transudation due to increased venous pressure
- » **Hepatic venous congestion symptoms**
 - Abdominal pain
 - Jaundice
- » **Other symptoms of organ congestion** (e.g., nausea, loss of appetite in congestive gastropathy)

General Physical examination findings

- » **Jugular venous distention:** visible swelling of the jugular veins due to an increase in CVP and venous congestion
- » **Kussmaul sign:** Paradoxical rise in JVP on inspiration
- » **Tender Hepatosplenomegaly**

Clinical features of left-sided heart failure (LHF)

Symptoms of pulmonary congestion

- » **Dyspnea** initially on exertion then at rest
- » **Orthopnea:** a sensation of shortness of breath that occurs upon lying down and is relieved by sitting up
- » **Paroxysmal Nocturnal Dyspnea:** Nocturnal bouts of coughing and acute shortness of breath, caused by reabsorption of peripheral edema at night → increased venous return

General Physical examination findings

- » Low volume pulse
- » Increased pulse rate
- » Decreased Blood pressure
- » Bilateral fine basal crackles/basilar rales may be audible on auscultation → Pulmonary edema
- » **Apex Beat:** Laterally displaced apical heart beat (precordial palpation beyond the midclavicular line)

APPROACH TO THE DIAGNOSIS OF HEART FAILURE

- All patients: Establish the diagnosis with routine blood test (CBC, LFTs, CRP, RFT, electrolytes), Fasting lipid profile, TSH, FBS and HbA1c in diabetic, cardiac biomarkers (Troponin, NT-pro-BNP), ECG, chest x-ray, and transthoracic echocardiogram.
- If CHF is confirmed, investigate for:
 - Underlying causes (consider coronary angiogram, chest imaging, and advanced cardiac imaging (Cardiac MRI, Cardiac Catheterization))
 - Modifiable risk factors: Hypertension, coronary artery disease

Diagnostic workup

BLOOD TEST	RADIOLOGICAL IMAGING
1. CBC: Anemia ($\downarrow$ Hb, $\downarrow$ MCV) and infection ($\uparrow$ WBCs). 2. RFTs: Creatinine = normal or $\uparrow$ 3. Serum Electrolytes: Na = normal or $\downarrow$ (hyponatremia can indicate a poor prognosis) 4. FBS/FBS or HbA1c: If diabetic or to rule out diabetes 5. LFTs: Elevations, particularly of the cholestatic enzymes, can indicate hepatic venous congestion 6. Inflammatory markers: $\uparrow$ CRP can indicate acute infection or inflammation 7. Fasting lipid profile: Elevated cholesterol 8. TFTs: $\downarrow$ TSH possibly sign of hyperthyroidism 9. Brain natriuretic peptide (BNP) < NT-proBNP NT-proBNP is a precursor of BNP; either can be used, as long as the correct values are used for interpretation • Release in response to pressure/volume overload, • High levels in patients with classic symptoms of CHF confirm the diagnosis (high predictive index). • High levels at discharge and no decrease during hospitalizations may signal worse outcomes. • Test of choice in early heart failure. • Uses for Evaluation of prognosis and disease severity (e.g., level at admission and predischarge) 10. Troponin T or I: Elevated levels can suggest ischemia but troponins can be elevated in CHF without acute myocardial ischemia and Potentially helpful for risk stratification	Transthoracic echocardiogram (TTE) best initial test to assess cardiac structure and function (to confirm EF, HF and also detect etiology) • Left ventricular systolic dysfunction: assessed via LVEF • HFpEF: normal (50–70%) • Borderline HFpEF: (41–49%) • HFrEF: reduced ($\leq 40\%$) • Diastolic dysfunction • Pulmonary hypertension and right ventricular dysfunction • Pericardial and/or pleural effusion • Evidence of complications: Cardiac dyssynchrony, Functional mitral regurgitation: Left atrial enlargement • Left ventricular hypertrophy in hypertension ECG: only shows right and left axis deviation Chest-X-ray: • Alveolar Edema • Enlarged: cardiothoracic width ratio > 0.5 • Boot-shaped heart on PA view: RV enlargement • Kerley-B lines (BAT wing appearance) • Dilated upper lobe vasculature • Signs of pericardial effusion (e.g., water bottle heart) • Obliteration of cardiophrenic & costophrenic angle Cardiac MRI: Gold standard for assessment of ventricular volume, mass, and ejection fraction, if Diagnostic uncertainty following echocardiography, detect congenital heart disease

DIAGNOSTIC EVALUATION OF HEART FAILURE

History	Symptoms	Examination	Diagnostic Tests
Family History	Dyspnea	Appearance	Chest Radiograph
Cardiovascular Disease History	Orthopnea/PND	Vital Signs	Electrocardiogram
Comorbidities	Bendopnea	Jugular Venous Distension	Echocardiogram
Relevant Exposures	Edema	Pulmonary Evaluation	Measurement of Natriuretic Peptide
	Fatigue	Cardiac Evaluation	Consideration of Additional Biomarker Testing
	Cognitive Dysfunction and Depression	Abdominal Evaluation	
	Chest Pain	Extremities Evaluation	Other Potential Tests
	Sleep Disorders		• Catheterization • Cardiac MRI • Hemodynamics • Exercise Capacity • Cardiac Biopsy

MEDICAL TREATMENT OF HEART FAILURE (HF) ACCORDING TO STAGES		
Stages	Treatment	Characteristics/Indication
Stage A	» ACEIs/ARBs	Treatment of cardiovascular risk factors
	» Beta-Blockers (BBs)	» Heart failure medications are not routinely recommended.
	» Statins	» Treat associated risk factors: Hypertension, Dyslipidemia, and Diabetes
Stage B	ACE inhibitors: » Enalapril » Lisinopril » Ramipril	» Every patient with HFrEF » Monitoring: BP, renal function, and potassium level 1–2 weeks after initiation or dose change
	Angiotensin receptor blockers » Losartan » Valsartan » Candesartan	» Patients who cannot tolerate ACEIs because of a dry cough » Monitoring: BP, renal function, and potassium level 1–2 weeks after initiation or dose change
	Beta blockers » Bisoprolol » Carvedilol » Metoprolol succinate	» Add once the patient is stable on ACEIs » Avoid in patients with decompensated HF until they are stabilized. » Monitoring ▪ Aim to titrate slowly to the target or maximum tolerated dose; if hypotension occurs, consider reducing the dose of ACEI to accommodate beta-blocker titration. ▪ Assess for symptoms of worsening HF or development of bradycardia
	Stage-B treatment PLUS with addition	
	Aldosterone antagonists » Spironolactone » Eplerenone	» All HFrEF patients with NYHA class II–IV symptoms and an LVEF of < 35% » Consider adding for patients with HFpEF. » Monitoring: regularly for hyperkalemia
Stage C	Loop diuretics » Furosemide » Bumetanide	» All patients with fluid retention » Begin treatment with loop diuretics to treat volume overload. » Thiazides may be added for a synergistic effect.
	Thiazide diuretics » Hydrochlorothiazide » Chlorthalidone	» Titrate the dose according to weight and volume status. » Regularly check electrolytes.
	Isosorbide dinitrate (ISDN) and Hydralazine	» Patients who cannot tolerate ACEIs or ARBs » Certain African American patients with HFrEF » Fixed-dose combination or Separate dosing of ISDN and hydralazine » Monitoring: volume depletion and hypotension
	Angiotensin receptor-neprilysin inhibitors (ARNIs) » Sacubitril/valsartan Combination (valsartan-sacubitril) Valsartan is an ARB, While sacubitril is a neprilysin inhibitor.	» HFrEF and persistent or worsening symptoms despite adequate treatment regimen with first-line drugs » Increased reduction in mortality compared to ACEI or ARB therapy » Initiation ▪ Stop ACEIs (elevated risk of angioedema otherwise). ▪ Administer ARNI no earlier than 36 hours after the last dose of ACEI. » Monitoring ▪ Monitor for hypotension, dizziness, or cough. ▪ Regular laboratory studies for hyperkalemia
	SGLT2 inhibitors » Dapagliflozin » Empagliflozin	» HFrEF with NYHA class II–IV symptoms » Administered in conjunction with first-line drugs » Reduction in cardiovascular mortality and hospitalization rates in patients with and without type 2 diabetes » Monitoring: GFR, Dehydration, hypotension & urogenital infection (UTI)
	Stage-B and C treatment PLUS with addition → Therapy for refractory symptoms	
	Digoxin	» HFrEF with persistent symptoms despite treatment with appropriate first-line medications. » Monitoring: renal impairment → RFTs
Stage D	Ivabradine	» If all of the following are present: ▪ NYHA class II–III ▪ Stable HFrEF ≤ 35% ▪ Sinus rhythm with Heart Rate of ≥70 bpm at rest on maximum tolerated beta-blocker dose » Monitoring: atrial fibrillation, bradycardia → ECG
	» Hepatojugular reflux: jugular venous congestion induced by exerting manual pressure over the patient's liver	
		» Coolness and palor of lower extremities

Implantable cardioverter defibrillator (ICD)	» consist of a pulse generator and leads that can sense VF or VT and deliver a shock to restore sinus rhythm
Biventricular pacing resynchronization	» Leads in the RA, RV, and coronary sinus (which lies adjacent to the LV) pace the heart in a coordinated manner.
Management of end-stage heart failure	
Inotropic support	» Used as a temporary measure to maintain organ perfusion in patients with cardiogenic shock
Mechanical circulatory support (MCS)	» Invasive devices used to support ventricular function » May be short-term (days to weeks) or long-term (months to years)
Heart Transplantation	» Definitive treatment

General Measure and Approach to the Management of Heart Failure (HF)

- Patient/family counselling:** Making sure that the patient understands the pathophysiological basis of the disease improves the effectiveness of treatment and quality of life.
- Lifestyle modification:** These interventions reduce general risk factors that are known to lead to the progression of CHF or other comorbidities (e.g., diabetes mellitus, hypertension).
 - » Restrict alcohol, optimise diet, weight loss and regular exercise
 - » Cessation of smoking, alcohol consumption, and recreational drug use
 - » **Salt restriction:** ≤ 1.5 g/day in stages-A and stage-B, ≤ 3 g/day in stages-C and stage-D
 - » Avoidance of potassium-rich foods while taking aldosterone antagonists
 - » **Fluid restriction:** 1.5 – 2 L/day in stage D patients who have edema and/or hyponatremia
- Treatment of comorbid/associated conditions:** The following conditions may worsen the symptoms of heart failure and accelerate progression.
 - » **Hypertension:** Treat with a target systolic blood pressure of < 130 mm Hg.
 - » **Dyslipidemia:** Start statins (Atorvastatin, Rosuvastatin) to keep lipids within the normal range.
 - » **Diabetes Mellitus:** Screen for Diabetes mellitus (FBS, HBA1C) and implement gradual glycemic control.
 - » Consider starting an SGLT2 inhibitors (Dapagliflozin, Empagliflozin)
 - » **Iron Deficiency Anemia (Normocytic-Normochromic):** send CBC, iron profile and start IV iron replacement with Inj. Ferric Carboxymaltose 500mg/10ml (FCM, Fercari)
 - » in patients with NYHA class II and III symptoms and iron deficiency
 - » **Obstructive Sleep Apnea:** Consider nocturnal continuous positive airway pressure (CPAP) therapy.
 - » **Atrial Fibrillation:** Start either rate or rhythm control and consider anticoagulation.
 - » **Coronary Artery Disease:** Consider coronary revascularization if there is concomitant IHD
 - » **Depression:** Sertraline (SSRIs) – safe in DM, IHD and Pregnancy as well
 - » **Hyperuricemia and gout** are common in heart failure and can be caused or aggravated by diuretic treatment. Acute gout attacks are better treated with colchicine, oral steroids, or intra-articular steroids rather than with an NSAID. Allopurinol can prevent gouty attacks more safely than Febuxostat.
- Avoidance of drugs that may worsen Congestive cardiac failure (CHF)**
 - » Most antiarrhythmic agents
 - » Calcium channel blockers (except Amlodipine and Felodipine)
 - » Non-Steroidal Anti-Inflammatory (NSAIDs) and cyclooxygenase-2 inhibitors
 - » Thiazolidinediones (Pioglitazone)
 - » Inhalation anesthetics
 - » **Cautious selection of antidepressants** due to numerous interactions and adverse effects when used with Heart failure drugs. **Tricyclic antidepressants should be avoided** because of their anticholinergic actions and potential to cause arrhythmias. **SSRIs are safe and well tolerated.**
 - » The combination of an ACE inhibitor, ARB, and aldosterone blocker that increases the risk of hyperkalemia.
- Start medical treatment based on heart failure staging.**
- Drugs that improve prognosis** are BBs, ACE inhibitors, ARNIs, aldosterone antagonists & hydralazine with nitrate.
- Diuretics and digoxin improve symptoms and significantly reduce the number of hospitalizations.
- Conducting regular serum electrolyte levels (K^+ & Na^+) is mandatory if the patient is taking diuretics
- Refer to cardiology for regular follow-up.



EVIDENCE-BASED TREATMENT OF HEART FAILURE

CURRENT MEDICAL DIAGNOSIS & TREATMENT (CMDT) 61TH 2023 EDITION & GOLDMAN-CECIL MEDICINE 26TH EDITION

Heart Failure with Reduced Left Ventricular EF (HFrEF)



- Hospitalized the patient
- Position of the patient should be propped up.
- Monitor vital signs and give 100% oxygen supplementation
- Correct underlying reversible etiology
- **Diuretics:** Regularly check serum electrolytes, titrate the dose according to weight and volume status.
 - » Inj. Furosemide 20mg/2ml (Lasix) at dosage 20mg to 120mg x IV x Stat than BD (max 20–320mg/day)
 - » Tab. Spironolactone 25mg (Aldactone-A) x OD or on alternate days (Maximum 25 to 50mg per day)
 - » OR Tab. Furosemide 20mg + Spironolactone 50mg (Spiromide) x 1/2 (Half) x OD
- **Dosage:** Start half tablet x Once daily than titrated, Target dose is one tablet once daily
- **Beta-Blockers (BBs):** Stable patients (defined as having no recent deterioration or evidence of volume overload) with mild, moderate, and even severe heart failure should be treated with a Beta-Blocker unless there is a non-cardiac contraindication. If Heart rate <50 beats/minute and worsening symptoms, halve dose of Beta-Blocker or, if severe deterioration, stop β -blocker (rarely necessary).
 - » Tab. Carvedilol 3.125mg or 6.25mg, 12.5mg or 25mg (Carveda, Carlov) x 3.125mg x BD
 - **Dosage:** Initiated at a dose of 3.125mg orally twice daily and may be increased to 6.25mg, 12.5mg, and 25mg twice daily at intervals of approximately 2 weeks.
 - **Available strength:** Tab. Carvedilol (Carveda, Carlov) 3.125mg, 6.25mg, 12.5mg and 25mg
 - » OR Tab. Metoprolol succinate 100mg (Betaloc-Zok) x 12.5 or 25mg (1/4th tab) x once daily
 - **Dosage:** Started at 12.5mg or 25mg x OD, Doubled at intervals of 2 weeks to a target dose of 200mg x OD
 - » OR Tab. Bisoprolol 2.5mg (Concor, Actim) x 1.25mg (Half tablet) x Once daily
 - **Dosage:** Initiated at a dose of 1.25mg, 2.5mg, 3.75mg, 5mg, 7.5mg, and 10mg x Orally daily, with increments at 1-to-4 week intervals.
 - **Available strength:** Tab. Bisoprolol (Concor, Actim) 2.5mg, 5mg and 25mg
- **Angiotensin-Converting Enzyme (ACE) Inhibitors:** Should be titrated over a period 1–3 months to target dose.
 - » Tab. Captopril 25mg or 50mg (Capoten, Capril) x initially 6.25mg x TDS titrated at target dose 50mg x TDS
 - » OR Tab. Lisinopril 5mg or 10mg (Zestril, Trupril) 2.5mg up to 5mg x OD titrated at target dose 10mg x OD
 - » OR Tab. Enalapril 5mg or 10mg (Renitec, Cortec) x 2.5mg x BD titrated at target dose 10mg x BD
 - » OR Tab. Ramipril 2.5mg (Ramipace, Tritace) 2.5mg up to 5mg x OD titrated at target dose 10mg x OD
 - **Available strength:** Tab. Ramipril (Ramipace, Tritace) 1.25mg, 2.5mg, 5mg and 10mg
- **Patients who cannot tolerate ACEIs because of a side-effect (dry cough) → Consider ARBs:**
 - » OR Tab. Candesartan 8mg or 16mg (Advant, Canrec) x Initially 4–8mg OD titrated up to 32mg x OD
 - » OR Tab. Losartan 50mg or 100mg (Eziday) x initially 50mg x OD titrated at target dose 150mg x OD
 - » OR Tab. Valsartan 80mg, 160mg (Exforge, Diovan) x 40mg (Half tab) x BD titrated up to 160mg x BD
- **Angiotensin Receptor-Neprilysin Inhibitors (ARNIs):** Combination of sacubitril/valsartan as a replacement first-line drug (ACEIs, Beta-Blockers & mineralocorticoid inhibitor) for patients with heart failure with reduced EF and persistent or worsening symptoms despite adequate treatment regimen with first-line drugs.
 - **Tab. Sacubitril 49mg + valsartan 51mg (Sacvin 49/51mg, Uperio 49/51mg) x initially 49/51mg x BD**
 - **Available strength:** Tab. Sacvin or Tab. Uperio 24/26mg (=50mg), 49/51mg (100mg) & 97/103mg (200mg)
 - **Dosage:** Starting dose usually sacubitril/valsartan 4/51mg twice daily if switching from ACE inhibitor/ARB (24/26mg twice daily if starting de novo), titrated at target dose up to 97/103mg x BD
 - **ACEIs treatment must be stopped for 36 hours before starting ARNIs (to minimize risk of angioedema)**
- **Sodium/glucose cotransporter-2 inhibitors (SGLT2i):** Reduction in cardiovascular mortality and hospitalization rates
 - » Tab. Dapagliflozin 10 mg (Forxiga, Dapa, Dapwiz) x Once daily
 - » OR Tab. Empagliflozin 10 mg (Empoli, Emglif, Jardiance) x Once daily
- **Ivabradine:** Ivabradine should be considered in patients who have persistent symptoms (NYHA class II to IV) despite treatment with a diuretic and other disease-modifying therapies (e.g., an ACE inhibitor [or ARB or ARNI], Beta-blocker, and a mineralocorticoid antagonist) and who are in sinus rhythm with a heart rate of 70 beats/min or greater.
 - » Tab. Ivabradine 5mg OR 7.5mg (Ivadin, Sivab) x started 5mg x OD and titrated to 7.5mg x OD
- **Consider Digoxin with HFrEF with persistent symptoms despite treatment with appropriate 1st line drugs**
 - » Tab. Digoxin 0.25mg (Lanoxin) x start at 0.125 mg or 0.25mg x OD on every alternate day
- **Monitoring of the serum digoxin concentration is recommended** because of the narrow therapeutic window. A steady state is reached 7 to 10 days after treatment is started; blood should be collected at least 6 hours (and ideally 8 to 24 hours) after the last dose. The currently recommended therapeutic range is 0.5 to 1.0 ng/mL. Digoxin can cause anorexia, nausea, arrhythmias, confusion, and visual disturbances, especially if the serum concentration is above 2.0 ng/mL.

Heart Failure with Preserved Left Ventricular EF (HFpEF)

- Hospitalized the patient
- Position of the patient should be propped up.
- Monitor vital signs and give 100% oxygen supplementation
- Correct underlying reversible etiology
- Diuretics:
 - Inj. Furosemide 20mg/2ml (Lasix) at dosage 20mg to 120mg x IV x Stat than BD (max 20—320mg/day)
 - Tab. Spironolactone 25mg (Aldactone-A) x OD or on alternate days (Maximum 25 to 50mg per day)
 - OR Tab. Furosemide 20mg + Spironolactone 50mg (Spiromide) x 1/2 (Half) x OD
 - **Dosage:** start half tablet x Once daily than titrated, Target dose is one tablet once daily
 - **Monitoring:** Regularly check serum electrolytes, titrate the dose according to weight and volume status.
- Beta-Blockers: Stable patients (defined as having no recent deterioration or evidence of volume overload) with mild, moderate, and even severe heart failure should be treated with a Beta-Blocker unless there is a non-cardiac contraindication. If Heart rate <50 beats/minute and worsening symptoms, halve dose of Beta-Blocker or, if severe deterioration, stop β -blocker (rarely necessary).
 - Tab. Carvedilol 3.125mg or 6.25mg, 12.5mg or 25mg (Carveda, Carlov) x 3.125mg x BD
 - **Dosage:** Initiated at a dose of 3.125mg x Orally twice daily and may be increased to 6.25mg, 12.5mg, and 25mg twice daily at intervals of approximately 2 weeks.
 - **Available strength:** Tab. Carvedilol (Carveda, Carlov) 3.125mg, 6.25mg, 12.5mg and 25mg
 - OR Tab. Metoprolol succinate 100mg (Betaloc-Zok) x 12.5 or 25mg (1/4th tab) x Once daily
 - **Dosage:** started at 12.5mg OR 25mg x OD, Doubled at intervals of 2 weeks to a target dose of 200mg x OD
 - OR Tab. Bisoprolol 2.5mg (Concor, Actim) x 1.25mg (Half tablet) x Once daily
 - **Dosage:** Initiated at a dose of 1.25mg, 2.5mg, 3.75mg, 5mg, 7.5mg, and 10 mg x Orally daily, with increments at 1-to 4-week intervals.
 - **Available strength:** Tab. Bisoprolol (Concor, Actim) 2.5 mg, 5 mg and 25 mg.

Important Guidelines

- ACE inhibitors and ARBs have not been shown to improve outcome in patients with heart failure and preserved LVEF, despite being good therapies of or the comorbidity of hypertension.
- Sacubitril/valsartan does not substantially improve outcome in patients with heart failure & preserved LVEF.
- Spironolactone has not been shown to improve outcome in a large trial of patients with HFpEF, but there may have been some benefit in patients enrolled in the Americas who had more clearly defined heart failure.
- Spironolactone should remain a therapeutic option, especially for patients who also have hypertension.
- Unlike in patients with heart failure and reduced LVEF, ICD and resynchronization device treatments do not have a role in patients with preserved LVEF.
- Revascularization of or patients with heart failure and preserved LVEF should be guided by the same considerations as of or patients with heart failure with reduced LVEF

PROGNOSIS OF HEART FAILURE

The prognosis depends on the patient, type and severity of heart disease, medication regimens, and lifestyle changes. The prognosis for patients with preserved EF is similar to or better than for patients with decreased EF. Risk stratification scales may be used to evaluate the prognosis (e.g., CHARM and CORONA risk scores).

Factors associated with worse prognosis

- Elevated BNP
- Hyponatremia
- Systolic BP < 120 mm Hg
- Diabetes
- Anemia
- Weight loss or underweight
- S3 heart sound
- Implantable cardioverter-defibrillator use
- Frequent hospitalizations due to CHF

1-year survival according to NYHA stage

- Stage-I: = 95%
- Stage-II: = 85%
- Stage-III: = 85%
- Stage-IV: = 35%

ACUTE HEART FAILURE (AHF)

Definition

- Acute heart failure: Rapid onset of new or worsening signs and symptoms of heart failure.
- Acute decompensated heart failure (ADHF): Acute heart failure due to decompensation of preexisting disease/cardiomyopathy (most common).
- De-novo heart failure: Acute heart failure occurring for the first time in a patient without known cardiomyopathy (=15% of cases).

Clinical features

Clinical features of acute heart failure are commonly classified according to perfusion and the presence of congestion at rest.

Classification of acute heart failure		
	No evidence of congestion (=5% of patients)	Evidence of congestion (=95% of patients)
Adequate perfusion	Warm and dry	Warm and wet
Hypoperfusion	Cold and dry	Cold and wet

Congestion (most common)

» Clinical features of left heart failure

- Acute dyspnea and orthopnea (i.e., worse when supine)
- Signs of increased work of breathing (WOB)
- Cough (occasionally with frothy, blood-tinged sputum)
- Coarse crackles/rales (and occasionally wheezing) on lung auscultation
- S3 gallop on heart auscultation
- Severe cases: central cyanosis

» Clinical features of right heart failure

- Jugular venous distention
- Hepatojugular reflux
- Peripheral edema
- Ascites
- Flash pulmonary edema: Typically manifests with hypertension, pulmonary congestion, and minimal peripheral edema

Hypoperfusion

- Weakness, fatigue, altered mental status
- Signs of poor peripheral perfusion: cold, clammy skin, peripheral cyanosis, skin mottling
- See also clinical features of "Cardiogenic shock."

Blood pressure: may be low, normal, or elevated and should be interpreted in relation to the patient's baseline BP

Diagnostic approach

- Acute heart failure (AHF) is primarily is clinical diagnosis
- Obtain natriuretic peptide, if the diagnosis is uncertain: NT-proBNP or BNP
- Evaluate clinically for possible triggers: missed medications, clinical features of ACS, infections
- Obtain chest x-ray to evaluate pulmonary congestion/pulmonary edema
- Order electrocardiography (ECG) and laboratory tests to investigate underlying conditions
- Arrange early TTE (Echo) for ADHF with a suspected decline in cardiac function OR any de novo heart failure.

Laboratory investigation

- NT-proBNP (or BNP): Useful for diagnostic confirmation and prognostication; can be measured serially to guide therapy. Should always be interpreted in comparison to the patient's baseline and in the context of history, examination, and radiological imaging. High diagnostic utility in patients with an unclear diagnosis

Natriuretic peptide levels in the diagnosis of heart failure			
	Heart failure unlikely	Heart failure likely	
BNP (pg/mL)	< 100	> 500	
NT-proBNP (pg/mL)	< 300	450, if <50 years old	900, if 50-75 years old
			1800 if >75 years old

» Additional routine blood tests

- Cardiac troponin-I: useful for detection ACS/Ischemia. Elevated level associated with poorer outcomes in AHF.
- The following lab test should be performed at admission in all patients with AHF: BUN/urea, serum creatinine, serum electrolytes, Complete blood count (CBC), Liver function test (LFTs)
- Thyroid profile (TSH level) and ABGs

TREATMENT OF ACUTE HEART FAILURE (AHF)

- ✓ Perform primary survey ABCD&E
- ✓ Provide respiratory support
 - » **Positioning:** Ensure the patient is sitting upright position with legs dangling over the side the bed full blown pulmonary edema.
 - » **Supplemental oxygen via mask:** indicated for patients with an $SpO_2 < 90\%$ OR $PaO_2 < 60$ mm Hg
- ✓ Establish intravenous line (IV cannula)
- ✓ Start continuous cardiac monitoring and **vitals monitoring:** B.P, P.R, R.R, Temperature, SpO_2 (pulse oximetry).
- ✓ **Obtained laboratory tests:** CBC, BUN, serum creatinine, serum electrolytes, LFTs, blood sugar, NT-proBNP (or BNP), serum troponin level, thyroid profile (TSH level) and ABGs
- ✓ Obtain chest x-ray, 12-lead Electrocardiogram (ECG) and arrange early transthoracic echocardiography (TTE).
- ✓ Provide supportive care:
 - » Restriction of fluid and sodium restriction
 - » Venous thromboembolism (VTE) prophylaxis
 - » Discontinue/avoid any cardiotoxic medications
- ✓ Initially start IV diuretic therapy:
 - » **Diuretics naïve patient (not exposed to diuretics):** Inj. Frusemide 20mg/2ml (Lasix) at dose 20–40mg IV over 1-2 minutes, may be repeated or increased by 20mg/dose every 1-2 hours until urine output increases & dyspnea improves. OR Bumetanide at dose 0.5mg – 1mg (Bumetanide 1mg = 40mg of frusemide)
 - » **Patients already taking diuretics:** Start 2.5 times the patient's usual oral dose intravenously as a bolus or continuous infusion.
- ✓ Continuing treatment IV diuretic therapy:
 - » **Dosage adjustment:** Assess the effect of diuretics (e.g., urine output, symptoms) every 6 hours.
 - » If urinary output is < 100 mL/hour: Consider doubling the diuretic dose.
 - » If urinary output is > 100 –150 mL/hour:
 - For patients with continued pulmonary edema: Continue scheduled diuretic at the current dose.
 - For patients with no residual pulmonary congestion/edema: Consider less frequent dosing or transition to an oral diuretic
 - » **Refractory AHF (despite high doses of loop diuretics):** Consider any of the following thiazide diuretics.
 - » Tab. Metolazone 5mg (Metxone, Metenix, Zaroxolyn) at dose 2.5 to 20mg PO once as needed
 - » OR Tab. Hydrochlorothiazide 25mg (Diuza) at dose 25mg – 50mg x twice daily
- ✓ Consider vasodilators → Glyceryl trinitrate (GTN) – Nitro 0.4mg spray x Translingual (apply the drug to the top of the patient's tongue) OR Tab. Angised 0.5mg x sublingually, provide immediate relief of effort angina. If pain do not settle in 5 minutes repeat GTN. Do not use vasodilators if Systolic BP is < 90 mm Hg.
- ✓ **IV Morphine:** it is not good choice for AHF due to its side-effects including the need for mechanical ventilation, prolonged hospitalization, ICU admission and mortality. If desired for its venodilation properties or pain control and with monitoring. According CMDT-2023, Morphine is highly effective in pulmonary edema and may be helpful in less severe decompensations when the patient is uncomfortable.
 - » Inj. Morphine 10mg/ml at dose of 2-8mg PLUS Inj. Metoclopramide 10mg/2ml (Metaclo), diluted in 0.9% N.S x IV (subcutaneous administration is effective in milder cases).
 - » May be repeated after 2–4 hours. Care must be taken if the patient has COPD/Asthma.
 - » **Dilution:** Morphine 10 mg/mL with 9mL 0.9% normal saline = 1mg/ml



☛ **If patient is hemodynamically unstable:**

- ☛ Admit to ICU/CCU
- ☛ Urgently cardiology consultation and critical care management.
- ☛ Consider invasive BLOOD PRESSURE monitoring.

☛ **If Respiratory failure – consider more aggressive respiratory support**

- ☛ **High-flow nasal cannula (HFNC):** Consider in patients with $SpO_2 < 90\%$ non-responsive to basic delivery systems.
- ☛ **NIPPV:** for patients with respiratory distress despite supplemental oxygen
 - BiPAP is preferred over CPAP.
 - Avoid in patients with isolated right ventricular failure, severe hypotension
- ☛ **Invasive mechanical ventilation:**
 - **Indications:** (1). Hypoxemic respiratory failure unresponsive to NIPPV, (2). Refractory hypoxemia ($PaO_2 < 60$ mm Hg), (3). Hypercapnia ($PaCO_2 > 50$ mm Hg)
 - Intubation and mechanical ventilation in patients with acute heart failure can be challenging.

☛ **Hemodynamic support management depends on the classification of AHF**

☛ **DRY AND COLD ACUTE HEART FAILURE (AHF)**

- Assess fluid responsiveness: Consider small fluid challenge then reevaluate volume status.
- If fluid responsive: Consider repeating fluid challenge.
- If signs of volume overload: Avoid fluids and optimize respiratory support for acute heart failure
- If shock refractory to fluids: Start vasopressor, ideally **Norepinephrine**
 - ☛ Inj. Norepinephrine at dose $0.05 - 0.4$ mcg/kg/minute x IV infusion, titrated as needed.
- If hypoperfusion persists despite fluids and vasopressor administration: Add inotropic support
 - ☛ Inj. Dobutamine at dose 2.5 mcg – 20 mcg/kg/minute x IV infusion, titrated as needed.

☛ **WET AND COLD ACUTE HEART FAILURE (AHF)**

- Start with inotropic support: IV Dobutamine, IV Dopamine, OR Milrinone
 - ☛ Inj. Dobutamine at dose 2.5 mcg – 20 mcg/kg/minute x IV infusion, titrated as needed.
 - Maximum rate at dose 40 mcg/kg/minute.
 - ☛ OR Inj. Dopamine at dose 5 mcg – 15 mcg/kg/minute x IV infusion, titrated as needed.
 - Maximum rate at dose 50 mcg/kg/minute.
 - ☛ OR Inj. Milrinone at dose 0.125 mcg – 0.75 mcg/kg/minute x IV infusion, titrated as needed.
 - Maximum rate at dose 0.75 mcg/kg/minute.
- If shock refractory to inotropes: Add a vasopressor – IV norepinephrine (Dose as mention above)

❖ **Dosages, dilution and IV infusion table are mention in the end of chapter**

- ☛ Monitor daily weights, strict intake/output, repeated monitoring and correction of serum electrolytes (e.g. potassium, magnesium, sodium) every 12-24 hours and serum creatinine (renal function) once daily
- ☛ **Identify and treat the underlying cause:** Acute MI, hypertensive crisis, thrombosis, infection, arrhythmia
- ☛ **Identify and treat comorbidities/complications:** Atrial fibrillation (A-fib) with RVR, Hyponatremia.
- ☛ Cardiology and nephrology consultation for AHF refractory to standard therapy (E.g., for peripheral ultrafiltration → modality to remove sodium and water in hospitalized patient with heart failure)
- ☛ Optimize medical therapy for congestive heart failure (CHF) once stable.

INFECTIVE ENDOCARDITIS (IE)

Clinical features

- » Constitutional Symptoms
 - » Fever and chills, tachycardia
 - » General malaise, weakness, weight loss, night sweats
 - » Dyspnea, cough, Pleuritic chest pain
 - » Arthralgias, Myalgias
- » Cardiac Manifestations
 - » Development of a new heart murmur or change in a preexisting murmur
 1. **Tricuspid valve regurgitation:** Holosystolic murmur that is loudest at the left sternal border → Seen in IV drug users, immunocompromised individuals, patients with congenital heart disease, and patients with instrumentation in the right heart (e.g., central venous catheters)
 2. **Aortic valve regurgitation:** early diastolic murmur that is loudest at the left sternal border
 3. **Mitral valve regurgitation:** holosystolic murmur that is loudest at the heart's apex & radiates to the left axilla
 - » Heart failure (Dyspnea, lower limb edema) due to valve insufficiency
 - » Arrhythmias: Suspect a perivalvular abscess in patients with infective endocarditis who develop a new conduction abnormality (e.g., heart block).
- » Extra-Cardiac Manifestations: Extracardiac symptoms are more common in left-sided IE, with the exception of pulmonary embolic manifestations, which are more common in right-sided infective endocarditis. These extracardiac manifestations are mainly caused by bacterial microemboli and/or the precipitation of immune complexes.
 - » **Petechiae**, especially **splinter hemorrhages** (hemorrhages underneath fingernails)
 - » **Janeway lesions:** Small, nontender, erythematous macules on palms and soles. Micro-abscesses with neutrophilic capillary infiltration and areas of hemorrhage caused by septic microemboli from valve vegetations
 - » **Osler nodes:** Painful nodules on pads of the fingers and toes caused by immune complex deposition
 - » **Roth spots:** Round retinal hemorrhages with pale centers
 - » **Emboli to intraabdominal organs**
 - **Acute renal injury (ARI)**
 - Including hematuria and anuria
 - Due to renal artery occlusion or glomerulonephritis
 - **Splenomegaly and possible left upper quadrant (LUQ) pain**
 - Due to splenic artery occlusion or splenic abscess
 - May lead to splenic rupture
 - » **Neurological manifestations (Seizures, Paresis):** due to septic embolic stroke, hemorrhages, meningitis, encephalitis, and/or cerebral abscess.
 - » **Signs of pulmonary embolism:** (Dyspnea) typically caused by septic emboli resulting from tricuspid valve involvement.
 - » **Arthritis:** Swelling and tenderness of one or more joints.

Classified by type of valve involved and clinical course

Clinical features	Native Valve Endocarditis		
	Acute Bacterial Endocarditis	Subacute Bacterial Endocarditis	Prosthetic Valve Endocarditis
	» Acute onset » Rapid, fulminant progression (days to weeks) » Severe constitutional symptoms (e.g., high fever)	» Insidious onset » Slow progression (weeks to months) » Less severe constitutional symptoms (e.g., low-grade fever, malaise, chills, dyspnea, back pain, weight loss)	» Early-onset: ≤1 year after surgery » Late-onset: > 1 year after surgery
Main pathogens	» Most common: Staph. aureus (associated with large vegetations that can destroy the valves) » Others: Group A hemolytic streptococci, S. pneumoniae, N. gonorrhoeae	» Viridans streptococci » Staph. aureus » Enterococci » HACEK bacteria	» Early-onset: Coagulase-negative staphylococci, S. aureus, or gram-negative bacilli (most common) » Late-onset: Coagulase-negative staphylococci, S. aureus, Viridans group streptococci (most common)
Affected valves	» Healthy native valves	» Native valves with prior injury or congenital defects	» Mechanical valves » Bioprosthetic valves

Classified by location of valves involved		
	Right-sided endocarditis	Left-sided endocarditis
Distinguishing clinical features	» Bacterial thromboemboli to pulmonary vasculature (e.g., due to lung abscess, pulmonary embolism) » Clinical features of right heart failure (e.g., peripheral pitting edema, abdominal pain from hepatic congestion) » Often associated with venous instrumentation (IV drug use, indwelling venous catheters)	» Emboli to systemic vasculature (See "Clinical manifestations" in "Clinical features") » Clinical features of left heart failure (e.g., dyspnea, pulmonary edema)
Main pathogens	» Staph. aureus (MSSA more often than MRSA) » Streptococci » Coagulase-negative staphylococci	» Staph. aureus » Viridans group streptococci » Community-acquired enterococci
Affected valves	» Tricuspid valve » Pulmonic valve	» Mitral valve » Aortic valve
Diagnostic approach		
Modified Duke criteria		
Criteria	Findings	
Major Criteria	1. Typical organisms from 2 separate blood cultures » Viridans streptococci » Staph. aureus » S. gallolyticus » HACEK group » Community-acquired enterococci without a primary focus » Persistently positive blood cultures with microorganisms consistent with endocarditis 2. ≥ 2 positive blood cultures drawn > 12 hours apart » All 3 or majority of ≥ 4 separate blood cultures » One positive blood culture for <i>Coxiella burnetii</i> OR a titer of anti-phase 1 IgG $\geq 1:800$ 3. Characteristic echocardiographic findings of infective endocarditis (IE) 4. New valvular regurgitation	
Minor Criteria	1. Predisposing condition (e.g., underlying heart abnormality, IV drug use) 2. Fever $> 38^{\circ}\text{C}$ (100.4°F) 3. Vascular abnormalities 4. Immunologic phenomena 5. Microbiology: Positive blood cultures not fulfilling major criteria or serological evidence of infection with common organisms	
Pathological	1. Microorganisms demonstrated by tissue culture or histology 2. Characteristic histologic features of active endocarditis	
Diagnostic category		
Definite IE if any of the following are present:	Possible IE if any of the following are present:	Rejected diagnosis if:
» ≥ 2 major criteria » ≥ 1 major criterion PLUS ≥ 3 minor criteria » ≥ 5 minor criteria » ≥ 1 pathological criterion	» ≥ 1 major criterion PLUS ≥ 1 minor criterion » ≥ 3 minor criteria	» Criteria for definite or possible IE not fulfilled » Firm alternative diagnosis present » Resolution of clinical characteristics in ≤ 4 days of antimicrobial therapy » Absence of surgical or autopsy evidence of IE
LABORATORY TEST		INVESTIGATION
» CBC: Leukocytosis with left shift » Inflammatory markers: $\uparrow$ CRP, $\uparrow$ ESR » Serum Urea, Creatinine (RFTs) and electrolytes: Assessment of renal function for antibiotic dosing » Blood cultures » Sampling protocol » Prior to treatment: 3 sets from different venipuncture sites » Monitoring: 2 sets every 24 – 48 hours until clearance » Interpretation » Positive bacterial cultures: Assess according to the modified Duke criteria. » Negative bacterial cultures do not rule out endocarditis. False negatives can be due to: 1. Antibiotic therapy prior to blood culture sampling 2. Fastidious bacteria (most commonly <i>Coxiella burnetii</i> and <i>Bartonella</i> spp.) 3. Fungal infection 4. Noninfective endocarditis		RADIOLOGICAL TEST Transthoracic echocardiography (TTE): TTE is the initial test of choice for all patients with suspected IE. It should ideally be performed within 12 hours of presentation and repeated after completing treatment. Transesophageal echocardiogram (TEE) is more invasive and is added in select cases. Indications for TEE include: » Presence of high-risk features » TTE findings inconclusive or suggestive of IE » Preoperative planning » Concern for intracardiac complications (abscess) Echocardiographic (TTE/TEE) findings fulfilling Duke criteria for IE » Valvular vegetations: Hyperechoic mobile masses located on the valve, mural endocardium, or prosthetic material » New valvular regurgitation (especially with valve prolapse, perforation, or destruction) » Prosthetic valve dehiscence and Perivalvular abscess Other high-risk findings include: Valve aneurysm, Fistula or pseudoaneurysm and Heart failure

Empiric antibiotic therapy for infective endocarditis

Valve type	Clinical presentation	Common antibiotic regimen
Native valve endocarditis	Acute bacterial endocarditis (days)	Vancomycin PLUS Cefepime
	Subacute bacterial endocarditis (weeks)	Vancomycin PLUS Ampicillin-sulbactam
Prosthetic valve endocarditis	≤ 1 year after valve placement	Vancomycin PLUS Gentamicin PLUS Rifampin PLUS Cefepime
	> 1 year after valve placement	Vancomycin PLUS Ceftriaxone

Targeted antimicrobial therapy for infective endocarditis

- Recommended for all patients
- Duration of therapy: Variable; can be ≥ 2 – 6 weeks after the first sterile blood culture.

Organism	Common antibiotic regimen for Native valve endocarditis	Common antibiotic regimen for Prosthetic valve endocarditis
Methicillin-susceptible staphylococci aureus (MSSA)	One of the following: Oxacillin or Nafcillin or Cefazolin	One of the following beta-lactams: Nafcillin or Oxacillin PLUS Rifampin PLUS Gentamicin
Methicillin-resistant staphylococci aureus (MRSA)	Vancomycin	Vancomycin PLUS Rifampin PLUS Gentamicin
Viridans group streptococci, S. gallolyticus	One of the following: Aqueous crystalline penicillin-G or Ceftriaxone PLUS (if resistant to penicillin) Gentamicin Alternative: Vancomycin 15-20 mg/kg IV every 8 – 12h × 6 weeks	
Enterococcus spp. (penicillin-sensitive)	One of the following: Ampicillin or Aqueous penicillin-G PLUS Gentamicin OR double beta-lactam therapy: Ampicillin PLUS Ceftriaxone	
Enterococcus spp. (penicillin-resistant)	Vancomycin PLUS gentamicin	
HACEK	Ceftriaxone Or Ampicillin+ Sulbactam	

Surgery of Infective Endocarditis

These procedures typically follow a multidisciplinary decision made by cardiology, cardiothoracic surgery, and infectious disease services.

Indications for surgical consultation include:

1. Prosthetic valve endocarditis
2. Valve dysfunction
3. Signs/symptoms of heart failure
4. New heart block
5. Annular or aortic abscess or destructive penetrating lesions
6. Fungal endocarditis
7. Complications secondary to perivalvular extension: Abscess, pseudoaneurysm, fistula

Surgical Options: valve replacement or valve repair

Complications

- Acute surgical complications: e.g., rebleeding from surgical sites, coagulopathy, acute renal failure, pneumonia
- Cardiac complications: e.g., CHF, myocarditis, pericarditis, new AV block
- Systemic emboli: e.g., stroke

Prevention of Infective Endocarditis

Endocarditis prophylaxis

Common indications

- Prior to the implantation of cardiac implantable electronic devices (e.g., AICD)
- Some dental procedures; in patients with high-risk cardiac features, such as:
 1. Prosthetic heart valves or prosthetic material used for valve repair
 2. History of endocarditis
 3. Types of congenital heart disease (CHD): unrepaired cyanotic CHD, Repaired CHD with shunt or regurgitation at or near the site of prosthetic material
 4. Cardiac transplant with valve regurgitation

Common regimens (usually administered 30–60 minutes prior to the procedure)

- Prior to cardiac device implantation: Cefazolin
- Prior to dental procedures
 - No penicillin allergy: Amoxicillin OR Ampicillin
 - Penicillin allergy: a macrolide (e.g., Azithromycin) OR Clindamycin



ACUTE RHEUMATIC FEVER & RHEUMATIC HEART DISEASE (RHD)

Name: _____ Age: _____ Sex: _____ Date: _____
 Temperature: _____ B.P: _____ Pulse: _____ Resp. Rate: _____

CLINICAL FEATURES

- ☞ Constitutional symptoms: Fever, Malaise, Fatigue
- ☞ Joints: Migratory Polyarthritis
- ☞ Heart
 - » Pancarditis (endocarditis, myocarditis, and pericarditis)
 - » Valvular lesions: most commonly on high-pressure valves
 1. Mitral valve (= 65% of cases):
 - ☞ Early mitral regurgitation or prolapse
 - ☞ Late mitral stenosis: Rheumatic fever is the most frequent cause of mitral stenosis.
 - ☞ Mixed mitral stenosis/regurgitation
 2. Aortic valve (= 25% of cases): Aortic regurgitation, Aortic stenosis (late manifestation)
 3. Tricuspid valve (= 10% of cases)
 4. Dilated cardiomyopathy due to severe valvular disease, myocarditis
- ☞ CNS: Sydenham chorea involuntary, irregular, non-repetitive movements of the limbs, neck, head, and/or face.
- ☞ Skin: Subcutaneous nodules and Erythema marginatum
 - ☞ Erythema marginatum: Centrifugally expanding pink or light red rash with a well-defined outer border and central clearing. Painless and nonpruritic. Location: The trunk and limbs are affected; the face is spared.

DIAGNOSTIC APPROACH

- ☞ Revised Jones criteria
 - » Diagnostic criteria for patients with laboratory findings of a preceding GAS infection
 - ✓ Initial episode of ARF: two major criteria or one major plus two minor criteria
 - » Recurrent ARF: either the same as for an initial episode of ARF or the presence of three minor criteria

MAJOR CRITERIA	MINOR CRITERIA
☞ Joints (Migratory Arthritis)	☞ Fever
☞ ♥ 'O' looks like the heart (Carditis)	☞ Antecedent strep infection
☞ Nodules (subcutaneous)	☞ Arthralgias
☞ Erythema marginatum	☞ ↑ Erythrocyte sedimentation rate (ESR)
☞ Sydenham chorea	☞ ↑ C-reactive protein (CRP)
☞ Mnemonic = Jones	☞ First-degree heart block

INVESTIGATION

- ☞ Routine test
 - » CBC: Typically shows leukocytosis, anemia
 - » Acute phase reactants
 - ☞ CRP: Elevated, typically ≥ 30 mg/L
 - ☞ ESR: Elevated, typically ≥ 60 mm/hour
 - » ECG: MC prolonged PR interval (first-degree AV block)
 - » X-ray: Enlarge Left atrium and ventricle, Pulm. edema
- ☞ Confirmation of GAS infection
 - » Tests showing elevated or rising antibodies
 - ☞ ↑ Antistreptolysin 'O' titer (ASO)
 - ☞ ↑ Antistreptococcal DNase-B titer (ADB)
 - » Positive throat culture
 - » Positive rapid GAS carbohydrate antigen detection test
- ☞ Echocardiography: MR > AR (Acute), MS (Chronic)

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC417888/>



Treatment of Acute rheumatic fever & Rheumatic heart disease (RHD)

- ☞ First line treatment: Inj. Benzathine penicillin G every 4 weeks for a minimum of 10 years, in patients with penicillin allergy, consider: Cap. Cephalexin 500mg (Ceporex) x 1 g per orally BD for 10 days or Azithromycin 500mg x OD x 5 days
- ☞ Symptomatic treatment of arthritis and fever
 - » NSAIDs: Treatment with an NSAID should continue until all symptoms of acute rheumatic fever have resolved.
 - ☞ Tab. Aspirin 300mg (Disprin) at dose 600mg (2 tablets) x 5-6 times daily [or at dose 50-60 mg/kg/day up to a maximum of 80-100 mg/kg/day (4-8g/day) for 3-4 weeks then tapered gradually depending on ESR/CRP level]
 - ☞ Alternative: OR Tab. Naproxen sodium 250-500mg (Flexin) x BD OR Tab. Ibuprofen 400mg (Brufen) x TDS orally once a day. (Maximum: 80mg/day). Not routinely recommended.
 - » Consider PPIs in patients at risk for GI bleeding: Tab. Pantoprazole 40mg (Zopent) x Orally once daily
- ☞ Carditis is treated as heart failure with diuretics (see acute heart failure), fluid restriction, salt restriction, and bed rest.
- ☞ Treatment of Sydenham chorea: Tab. Carbamazepine at dose 3.5-10 mg/kg/dose orally BD OR Tab. Sodium valproate at dose 7.5-10 mg/kg/dose orally BD, if severe addition of Tab. Prednisolone 1-2mg/kg/day x BD (Maximum 80mg/kg/day)
- ☞ Prophylaxis: Inj. Benzathine penicillin-G 1.2 million (Benzibiotic) x every 4 weeks for a minimum of 5 years (if there is no cardiac involvement) OR 10 years (if there is cardiac involvement) after the last acute rheumatic fever episode.

PERICARDITIS

Name: _____ Age: _____ Sex: _____ Date: _____
 Temperature: _____ B.P: _____ Pulse: _____ Resp. Rate: _____

- Acute pericarditis: Inflammation of the pericardium that either occurs as an isolated process or with concurrent myocarditis (myopericarditis = Predominantly affecting the myocardium with pericardial involvement)
- Chronic pericarditis: inflammation of the pericardium that lasts > 3 months
- Constrictive pericarditis is characterized by compromised cardiac function caused by a thickened, rigid, and fibrous pericardium secondary to acute pericarditis.

Etiology

- | | |
|--|--|
| 1. Infections <ul style="list-style-type: none"> » Virus: Coxsackieviruses (commonest), influenza, EBV, CMV, ECHO-viruses, mumps & measles virus » Bacterial: Mycoplasma, Pneumococcus, mycobacterium tuberculosis, staphylococcus, streptococcus, H.Influenza. » Parasite: Amebiasis » Fungi: Histoplasma, Blastomycosis, Candida | 2. Inflammation <ul style="list-style-type: none"> » Autoimmune disorders: systemic lupus erythematosus (SLE), Rheumatoid arthritis, systemic sclerosis, ankylosing spondylitis, sjogren syndrome. » Medications: Hydralazine Isoniazid, Penicillamine, methyldopa (Drug induced SLE) » Miscellaneous: Idiopathic, Dressler syndrome (Post-MI pericarditis), Radiations, Amyloidosis. |
| 3. Hemopericardium: Bleeding in pericardial space <ul style="list-style-type: none"> » Cardiac wall rupture: Complication of MI » Chest trauma: Traumatic cardiac tamponade » Aortic dissection » Cardiac surgery: Heart valve surgery, coronary bypass surgery » Bleeding disorder: DIC, ITP, WVD | 4. Other causes: <ul style="list-style-type: none"> » Malignancy » Medications: Aspirin, warfarin, heparin » Uremia » Postpericardiotomy syndrome » Hypothyroidism » Right heart failure |

Morphological classification of Pericarditis

Types	Etiology	Outcome
Serous pericarditis	» Viral infection	» Resolve itself
Fibrinous pericarditis	» Autoimmune disorder (e.g., SLE, RA), drugs, irradiation, uremia, Dressler syndrome	» Resolves » Or leading to adhesive pericarditis
Haemorrhagic pericarditis	» Post cardiac surgery, malignancy, trauma, cardiac rupture, bleeding disorders	» Resolves » Or leading to adhesive pericarditis
Mucopurulent pericarditis	» Bacterial infection, Tuberculosis	» Adhesive pericarditis » Constrictive pericarditis
Caseous pericarditis	» Tuberculosis	» Calcified pericarditis or fibrosis » Constrictive pericarditis

Clinical features

- Chest pain
 - » Pleuritic chest pain
 - Acute, sharp retrosternal pain caused by inflammation of the parietal pleura
 - Typically aggravated by deep breathing, movement, a change of position, exercise and swallowing.
 - Other causes of pleuritic chest pain include myocardial infarction, pulmonary embolism, and pneumothorax.
 - » Improves on sitting and leaning forward
 - » Can radiate to the neck and shoulders (most commonly to the left side)

- Pericardial friction rub: **High-pitched, superficial scratching or crunching noise**, produced by movement of the inflamed pericardium on auscultation and is **diagnostic of pericarditis** (Present in 85% of patients)
 - Indicates friction between the visceral and parietal pericardial tissue
 - Best heard over the left sternal border during expiration while the patient is sitting up and leaning forward
 - Occurs in atrial and ventricular systole, but may also be audible in early diastole.
- Pericardial effusion: Faint/Muffled heart sound and **Ewart sign** (Dullness to percussion at the base of the left lung with increased vocal fremitus & bronchial breathing due the compression of lung parenchyma by the pericardial effusion)
- Fever: Low-grade intermittent fever are common
- Additional features: Tachypnea, dyspnea, dizziness, palpitation, non-productive dry cough

Diagnostic approach

- The diagnosis can often be made on the basis of clinical features and the ECG. Rule out other causes of acute chest pain (MI, myocarditis and pulmonary embolism) before making a diagnosis of acute pericarditis
- Diagnostic criteria for acute pericarditis:**
 - At least two of the following four criteria must be present for a diagnosis of acute pericarditis:
 - Characteristic chest pain
 - Pericardial friction rub
 - Typical ECG changes:** ST elevation with upward concavity
 - New or worsening pericardial effusion
- ECG features of pericarditis:** ST elevation with upward concavity (diffuse ST elevations) over the affected area, which may be widespread. PR interval depression is a very specific indicator of acute pericarditis. Later, there may be T-wave inversion, particularly if there is a degree of myocarditis.
- Echocardiography:** May be normal in pericarditis or may reveal pericardial effusion and pericardial tamponade
- CT scan with IV contrast and cardiac MRI** – Consider if the diagnosis is uncertain.
- Chest x-ray:** usually normal; may show an enlarged cardiac silhouette
- Laboratory investigation**
 - Elevation of inflammatory markers may support the diagnosis of pericarditis but are not considered to be a part of the diagnostic criteria: **CBC:** Leukocytosis, **Troponin-i:** ↑, **Serum ESR:** ↑, **Serum CRP:** ↑ and **Serum Creatinine kinase (CK):** ↑
 - Pericardiocentesis with pericardial fluid analysis**
 - Indications:** large effusion, tamponade, suspected malignant or purulent pericarditis
 - Investigations depend on suspected etiology:** Gram stain, Bacterial culture, Acid-fast bacilli smear microscopy and culture, PCR and Cytology
 - Additional workup based on suspected etiology**
 - Uremic pericarditis:** BUN/Urea, serum creatinine, serum electrolytes, Renal ultrasound
 - Bacterial pericarditis:** Blood cultures (2 sets)
 - Tuberculous pericarditis:** Quanti-FERON TB assay/PPT kit test, HIV test & Chest x-ray
 - Autoimmune pericarditis:** ANA, rheumatoid factor

DIAGNOSTIC FEATURES OF "DRY PERICARDITIS" VS "WET PERICARDITIS"

DRY PERICARDITIS	WET PERICARDITIS																	
» Pleuritic chest pain + Fever » Pericardial rub on auscultation precardium » ECG: » Stage 1: ST elevation with upward concavity » Stage 2: ST segment normalizes in = 1 week. » Stage 3: inverted T waves » Stage 4: ECG returns to normal baseline (as prior to onset of pericarditis) after weeks to months. » Chest X-ray (CXR): Usually normal » Echocardiography: Usually normal	» Pleuritic chest pain + Fever » Muffled heart sound on auscultation precardium » ECG: Low voltage complexes (P, QRS and T wave) » CXR: Globular-shaped heart and sharp cardiophrenic angles » Echocardiography:<table><tr><th>Grade/size</th><th>Pericardium & epicardium diameter in diastole</th><th>Volume</th></tr><tr><td>Trivial</td><td>Seen only in systole</td><td>< 50 mL</td></tr><tr><td>Small effusion</td><td>< 10 mm echo free space</td><td>50 – 100 mL</td></tr><tr><td>Moderate effusion</td><td>10–20 mm echo free space</td><td>100 – 500 mL</td></tr><tr><td>Larger effusion</td><td>20 mm echo free space</td><td>> 500 mL</td></tr></table>			Grade/size	Pericardium & epicardium diameter in diastole	Volume	Trivial	Seen only in systole	< 50 mL	Small effusion	< 10 mm echo free space	50 – 100 mL	Moderate effusion	10–20 mm echo free space	100 – 500 mL	Larger effusion	20 mm echo free space	> 500 mL
Grade/size	Pericardium & epicardium diameter in diastole	Volume																
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Small effusion	< 10 mm echo free space	50 – 100 mL																
Moderate effusion	10–20 mm echo free space	100 – 500 mL																
Larger effusion	20 mm echo free space	> 500 mL																

TREATMENT OF PERICARDITIS

Rx

- ✓ Perform primary survey ABCD&E
- ✓ Provide supplemental oxygen via mask: indicated for patients with an $SpO_2 < 90\%$
- ✓ Establish intravenous line (IV cannula)
- ✓ Vitals monitoring: B.P, P.R, R.R, Temperature, SpO_2 (pulse oximetry).
- ✓ Send laboratory tests: CBC, BUN, serum creatinine, serum electrolytes, LFTs, FBS, NT-proBNP (or BNP), troponin-i level, Creatinine kinase, ESR, CRP, thyroid profile (TSH level) and ABGs
- ✓ Obtain Chest x-ray, 12-lead Electrocardiogram (ECG) and arrange early transthoracic echocardiography (TTE).
- ✓ Rule out life-threatening differential diagnoses of chest pain.
- ✓ Immediate pericardiocentesis in unstable patients if there is evidence of tamponade
- ✓ Start NSAIDs: (if there are no contraindications to NSAIDs).
 - ✎ Tab. Aspirin 300mg (Disprin) at dose 600mg x 6 times daily
 - OR Tab. Ibuprofen 400mg (Brufen) at dose 200mg – 800mg orally every 6-8 hours.
 - OR Cap. Indomethacin 50mg (Indobid) at dose 100mg (2 capsule) 3 times daily
 - » More potent anti-inflammatory
- ✓ Corticosteroids (prednisolone): Treatment can alternatively be used for patients with poor NSAIDs tolerance. It is used in severe cases or in pericarditis caused by uremia, connective tissue disease, or autoreactivity.
- ✓ Consider colchicine in combination with NSAIDs or as a monotherapy:
 - ✎ Tab. Colchicine 0.5mg orally twice, maybe beneficial adjuvant and may prevent recurrent episodes and symptoms persistent at 72 hours.
- ✓ Consider PPIs in patients at risk for GI bleeding
 - ✎ Cap. Pantoprazole 40mg (Zopent) x Orally once daily
 - OR Cap. Dexlansoprazole 30mg OR 60mg (Dextop, Dolgina, Dexiva) x Orally once daily
- ✓ Supportive therapy
 - » Identify and treat the underlying cause.
 - » Empiric IV antibiotic therapy for bacterial cause: Inj. Ceftriaxone 1-2g (Oxidil) x IV PLUS Inj. Vancomycin 1g (15mg/kg) x IV x BD or Inj. Meropenem 1g (Meronem) x TDS
 - » Tuberculosis therapy: Anti-tubercular therapy (See management of tuberculosis)
 - » Immunosuppressants in autoimmune disease
 - » Dialysis in the case of uremia
- ✓ Advise patients to limit strenuous exercise/restrict physical activity in patients with acute pericarditis x 6mon
- ✓ If heart failure present initiate diuretics: Inj. Furosemide 40mg/2ml (Lasix) at dose 20 to 80mg x IV, repeat and titrated as needed.
- ✓ Consider cardiology consultation for severe cases.
- ✓ Consider admission in severe cases.
- ✓ If the patient is discharged, arrange for a follow-up in 1 week.



PERICARDIAL EFFUSION AND CARDIAC TAMPONADE

- Pericardial effusion:** an accumulation of fluid in the pericardial space between the parietal and visceral pericardium. Pericardial effusion may be acute or chronic.
- Cardiac tamponade:** This term is used to describe acute heart failure due to elevated intra-pericardial pressure from large pericardial effusion causes compression of the heart especially the right ventricle. Tamponade may complicate any form of pericarditis but can be caused by malignant disease, by blood in the pericardial space following trauma, or by rupture of the free wall of the myocardium following MI.

Risk factor/Etiology

- Hemopericardium:** Bleeding in pericardial space
- » Cardiac wall rupture: Complication of MI
 - » Penetrating chest trauma – Traumatic cardiac tamponade
 - » Aortic dissection
 - » Cardiac surgery:
 - ↳ Iatrogenic (Invasive procedure)
 - ↳ Heart valve surgery
 - ↳ Coronary bypass surgery
 - » Bleeding disorder: DIC, ITP, VWD
- Serous or serosanguinous pericardial effusion**
- » Idiopathic
 - » Infections: pericarditis (acute, uremic, constrictive), tuberculosis, myocarditis, and Restrictive CMP.
 - » Postpericardiotomy syndrome
 - » Cancer/malignancy
 - » connective tissue disorders
 - » Autoimmune disorders (SLE)
 - » Hypothyroidism
 - » Right heart failure

Clinical features

- | Pericardial effusion | Cardiac Tamponade |
|---|---|
| Initially asymptomatic in most cases | Symptoms are sudden onset of cardiovascular collapse and may be associated with chest pain, Dyspnea, tachypnoea, fatigability, Restlessness. |
| Shortness of breath on lying down (orthopnea) | If more severe cases: dizziness, syncope, obstructive shock, altered mental state and cardiac arrest |
| Retrosternal chest pain <ul style="list-style-type: none"> ↳ Radiate to left shoulder, sharp, ↑ by lying down. ↳ Relieved by bending forward and sitting forearm. | Classical finding of cardiac tamponade – Beck's triad: <ol style="list-style-type: none"> 1. Hypotension, 2. Muffled heart sounds 3. Distended neck veins (Increase JVP) |
| Symptoms due to compression of adjacent structure: <ul style="list-style-type: none"> ↳ Dyspnea ↳ Dysphagia, hoarseness ↳ Nausea ↳ Hiccups | Tachycardia, Pallor/cyanosis, cold sweats |
| Apical impulse is difficult to locate or non-palpable. | Pulsus paradoxus: define as a decrease > 10 mmHg in systolic pressure during inspiration. |
| Ewart sign: dullness to percussion at the base of the left lung with ↑ vocal fremitus & bronchial breathing due the compression of lung parenchyma by the pericardial effusion | Kussmaul sign - a paradoxical elevated in JVP & pressure during inspiration |
| Symptoms of right heart failure (RHF) maybe present | Friedreich sign – JVP sharp diastolic collapse (x & y wave) |

Diagnostic studies

- Chest x-ray P.A view:** can suggest cardiomegaly (globular-shaped heart) → massive pleural effusion. If no cardiomegaly then rule out restrictive cardiomyopathy. If calcified spots on heart → tuberculosis causes constrictive pericarditis
- Electrocardiography (ECG):** Indicated in all patients. May show features of the underlying disease (pericarditis or acute MI).
- ↳ Findings in pericardial effusion: ECG usually normal in smaller pericardial effusions, Low voltage complexes and electrical alternans in larger pericardial effusions
 - ↳ Findings in cardiac tamponade: ECG often reveals sinus tachycardia, low voltage QRS complexes and Electrical alternans
- Echocardiography:** Quick and safe for diagnosis, classification and monitoring.
- Transthoracic echocardiography (TTE)** is gold standard
- Findings supportive of pericardial effusion:** A pericardial effusion appears as a transparent separation between the parietal and visceral pericardium during the cardiac cycle.

Grade/size	Free space between the pericardium & epicardium in diastole	Volume
Trivial	Seen only in systole	
Small effusion	< 10 mm	< 50 mL
Moderate effusion	10–20 mm	50 – 100 mL
Larger effusion	20 mm	100 – 500 mL
		> 500 mL

- Findings supportive of cardiac tamponade:** If tamponade is present, the high intra-pericardial pressure may collapse lower pressure cardiac structures, such as the RA and RV.
- ↳ Chamber collapse
 - Early signs: collapse of the right atrium during systole; collapse of the right ventricle during early diastole
 - Later: collapse of the left atrium
 - ↳ Swinging motion of the heart
 - Inspiration: decrease in LV filling

- Exhalation: increase in LV filling and decrease in RV filling
- Cardiac CT scan: Demonstrate pericardial fluid, pericardial thickening, & any associated contiguous lesions within the chest
- Diagnostic pericardiocentesis: Pericardial effusion of unclear etiology → Pericardial fluid analysis
- Laboratory test and specific investigations
 - CBC: Leukocytosis if infection or inflammation
 - Serum CRP & ESR: Elevated in infection or inflammation
 - Troponin-I: Can be slightly elevated in pericarditis, significantly elevated if there is associated myocarditis
 - Creatinine kinase (CK): Elevated in myocarditis, rhabdomyolysis
 - BUN/Urea: elevated in uremic pericarditis
 - Coagulation profile
- Additional investigation of underlying etiology in pericardial effusion
 - Acute pericarditis: Blood cultures, If TB is suspected – Quanti-FERON TB assay/PPT kit test, HIV test & Chest x-ray
 - Uremic pericarditis: Renal ultrasound
 - Autoimmune disease: ANA, Rheumatoid factor, ACPA, ANCA, Ferritin & specific radiograph if required
 - Malignancy: Serum calcium, CT scan, PET scan
 - Hypothyroidism: Thyroid function tests (TSH, free t4, free t3) & Thyroid ultrasound
 - Aortic dissection: D-dimer, CT angiography
 - Postpericardiotomy syndrome: Blood cultures, Chest x-ray
 - Trauma: FAST scan, Trauma CT scan and Additional x-rays as required

Treatment approach of pericardial effusion and cardiac tamponade

Cardiac tamponade is a medical emergency: When the diagnosis is confirmed, urgent percutaneous pericardiocentesis should be performed, which usually results in a dramatic improvement.

- Perform primary survey ABCD&E
- Provide supplemental oxygen via mask: indicated for patients with an SpO₂ < 90%
- Bed rest with legs elevated.
- Establish intravenous line (IV cannula)
- Vitals monitoring: B.P, P.R, R.R, Temperature, SpO₂ (pulse oximetry).
- Send laboratory tests: CBC, BUN, serum creatinine, serum electrolytes, LFTs, FBS, NT-proBNP (or BNP), troponin-I level, Creatinine kinase (CK), ESR, CRP, thyroid profile (TSH level) and ABGs
- Unstable patients: Identify and treat cardiac tamponade urgently, if present.
- Stable patients
 - Small pericardial effusion: can be followed by clinically by careful observation. Conservative management focusing on treating the underlying cause is usually sufficient.
 - Large effusion causing symptoms or of uncertain etiology: Consider pericardial fluid drainage.
- All patients
 - Treat the underlying cause: Management acute heart failure and treat pericarditis.
 - Provide supportive care: Pain and fever management
- Disposition
 - Urgent cardiology consultation is required, if cardiac tamponade is suspected → Urgent pericardiocentesis or cardiac surgical procedure are required.
 - Consult cardiothoracic surgery if surgical pericardial fluid drainage is indicated.
 - If pericardiocentesis is performed, admit patients to hospital ward or observation unit for post-procedure monitoring, serial examination, and pericardial fluid analysis.

PERICARDIAL FLUID DRAINAGE

- Therapeutic pericardiocentesis
 - Performed as a temporizing measure for hemodynamically unstable patients with cardiac tamponade
 - Can relieve symptoms for large chronic or recurrent effusions
 - Consider specialist referral for patients at high risk of re-accumulating pericardial fluid, e.g., for indwelling catheter or pericardiectomy
- Pericardiectomy: the creation of an opening in the pericardium to allow continuous drainage of pericardial fluid (externally or into the pleural space)
 - Surgical pericardiectomy (pericardial window): A surgical incision is made in the pericardium.
 - Subxiphoid approach: can be done under local anesthesia at the bedside (e.g., emergency department or ICU) and allows external fluid drainage
 - Thoracotomy approach: needs to be done in the operating room and allows drainage into the pleural cavity

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- » **Percutaneous balloon pericardiotomy:** A transthoracic needle introduces a balloon-tipped catheter into the pericardial space which is progressively dilated to create an opening wide enough for continuous drainage.
- » **Complications:** The mortality rate varies from 8–19%, depending on the underlying etiology.
- » **Pericardiectomy:** performed as definitive management for refractory pericardial effusion, effusion due to constrictive pericarditis, or purulent pericarditis

APPROACH TO THE MANAGEMENT OF CARDIAC TAMPONADE

- » **Rapid evaluation of unstable patients:** Cardiac tamponade is a clinical diagnosis, however, clinical features are poorly sensitive and the diagnosis is often confirmed retrospectively.
 - » Use POCUS to confirm the presence of a pericardial effusion.
 - » Suspect tamponade in patients with suggestive clinical features and/or bedside imaging findings.
 - » $\geq 70\%$ of patients have ≥ 1 of the following:
 1. Shortness of breath
 2. $\uparrow$ Heart rate
 3. $\uparrow$ JVP
 4. Pulsus paradoxus (> 10 – 12 mm Hg)
 5. Cardiac enlargement on CXR
 - » Beck's triad is poorly sensitive for tamponade and it is very rare for all elements to be present.
 - » $< 50\%$ of patients have low voltage QRS complexes on ECG.
 - » Obtain an urgent bedside echocardiography to evaluate cardiac tamponade.
 - » Evaluate the need for immediate pericardial fluid drainage.
 - » Consult a cardiologist and/or cardiothoracic surgeon and consider using a scoring system to help determine when urgent pericardiocentesis is advised and when it can safely be deferred.
- » **Cardiac arrest due to suspected cardiac tamponade**
 - » **Nontraumatic cardiac arrest**
 - Consider POCUS (Point of care USG) during CPR to confirm pericardial effusion.
 - Pause CPR to perform immediate pericardiocentesis as soon as possible if cardiac tamponade is the suspected etiology.
 - Blind pericardiocentesis can be performed using landmarks if no ultrasound guidance is available.
 - » **Traumatic cardiac arrest**
 - Assume pericardial fluid seen on FAST scan is traumatic hemopericardium.
 - Perform emergency thoracotomy with vertical pericardiotomy.
- » **Urgent pericardial fluid drainage**
 - » Perform pericardiocentesis under echocardiographic (or fluoroscopic) guidance without delay in unstable patients unless indications for immediate surgery are present.
 - » Do not delay immediate surgical management in patients with a low likelihood of successful pericardiocentesis due to immediate reaccumulation of pericardial fluid, for example in:
 1. Type A aortic dissection
 2. Ventricular free wall rupture
 3. Severe blunt chest trauma or penetrating chest injury
 4. Iatrogenic hemopericardium refractory to percutaneous hemostatic control
 - » Refer for surgical management if pericardiocentesis is unsuccessful, e.g., due to difficult conditions
- » **Hemodynamic support** $\rightarrow$ Manage as obstructive shock.
 - » Maintain IV access with 2 large-bore IV lines (peripheral or central).
 - » Cautious fluid resuscitation (only in hypovolemic patients)
 - » **Inotropic support:** Inj. Dobutamine
 - » Avoid anesthetic agents and positive pressure ventilation.
- » **Subsequent management**
 - » Identify and treat the underlying cause.
 - » **Empiric broad-spectrum antibiotics:**
 - » Inj. Ceftriaxone 1-2g (Oxidil, Titan, Rocehin) x IV
 - PLUS Inj. Vancomycin 1g (at dose 15mg/kg) x IV x BD
 - OR Inj. Meropenem 1g (Meronem) x TDS
 - » Monitor for complications and reaccumulation.
 - » ICU/CCU admission is recommended
 - » Continuous telemetry/cardiac monitoring
 - » Regular Blood Pressure monitoring
 - » Serial pulsus paradoxus measurement

CARDIOMYOPATHIES

Name: _____ Age: _____ Sex: _____ Date: _____
 Temperature: _____ B.P: _____ Pulse: _____ Resp. Rate: _____

Definition: Cardiomyopathies are group of disorders which is characterized by primary abnormality in myocardium.

Classification of cardiomyopathies:

- » Dilated cardiomyopathy (DCM)
- » Hypertrophic obstructive cardiomyopathy (HOCM)
- » Restrictive cardiomyopathy
- » Arrhythmogenic right ventricular cardiomyopathy (ARVS)

DILATED CARDIOMYOPATHY (DCM)

- » **Clinical definition:** Dilated cardiomyopathy (DCM) is progressive myocardial hypertrophy and dilation leading to systolic dysfunction. It is the most common type of non-ischemic cardiomyopathy and a common cause of heart failure (HF).
- » **Most common indication for heart transplant**

ETIOLOGY

- » **Mostly idiopathic (50%)**
- » **Familial (25%) → Genetic mutations:** affect proteins in the cytoskeleton of the myocytes, such as dystrophin, lamin A & C, titin (TTN), MYH7, emerin & metavinculin
- » Ischemic heart disease (IHD)
- » Untreated hypertension
- » Long standing valvular heart disease (MR or AR)
- » **Infectious diseases:** Coxsackie-B viral myocarditis, Chagas disease (by protozoa *Typanosoma cruzi*) and HIV
- » **Autoimmune disorders (SLE), sarcoidosis & hemochromatosis**
- » **Endocrinopathies:** hypothyroidism, hyperthyroidism, acromegaly, pheochromocytoma
- » **Nutritional:** Thiamine deficiency (wet beriberi), selenium
- » **Substance use:** Alcohol abuse, Chronic cocaine, amphetamine
- » **Medication:** Doxorubicin, Daunorubicin, Anti-cancers
- » **Tachycardia induced:** Hyperthyroidism/thyroid dysfunction, Peripartum cardiomyopathy, Iron deficiency anemia (IDA)
- » **Stress:** Takutsubo cardiomyopathy or broken heart syndrome

PATHOGENESIS

- » Causative factors decrease the contractility of the myocardium → activation of compensatory mechanisms (Frank-Starling law) to maintain cardiac output → ↑ end-diastolic volume (preload) → myocardial remodeling → **eccentric hypertrophy & dilation of the ventricle**; → reduced myocardial contractility → systolic dysfunction & ↓ ejection fraction → heart failure.
- » Decreased LV contractility due to dilation leads to left heart failure and eventually right heart failure

CLINICAL FEATURES

- | | |
|---|--|
| <ul style="list-style-type: none"> » Symptoms <ul style="list-style-type: none"> » Gradual development of symptoms of congestive heart failure (CHF) <ul style="list-style-type: none"> ▪ Dyspnea ▪ Ankle/sacral edema ▪ Chest pain ▪ Palpitation ▪ Productive cough ▪ Dizziness, faintness, fatigue » Some patients may present with symptoms of arrhythmia. | <ul style="list-style-type: none"> » Physical examination <ul style="list-style-type: none"> » Systolic murmur secondary to MR or TR » S3 gallop rhythm on auscultation » Displacement of the apex beat » Lungs: Bilateral fine basal crepitation/basilar rales may be audible → Pulmonary edema » Jugular venous distention (Elevated JVP) » Lungs: Bilateral fine basal crepitation/rales » Peripheral edema, Ascites and tender hepatomegaly » In severe cardiac failure: Cheyne-Stokes breathing, pulsus alternans, pallor, and cyanosis may be present. |
|---|--|

DIAGNOSTIC WORKUP

- » Most patient's diagnosis during the workup for associated cardiac conditions such as heart failure or are found to have the condition during routine investigation or through screening of family members of patients with known or suspected familial dilated cardiomyopathy (DCM)
- » **Initial laboratory test**
 - » CBC with differential
 - » Liver function tests (LFTs)
 - » Serum BUN/urea
 - » Serum creatinine
 - » Serum electrolytes
 - » Serum TSH
 - » HIV testing
 - » **Iron profile:** Ferritin, transferrin saturation
 - » **BNP or NT pro-BNP:** To help establish prognosis and disease severity in CHF



Additional test as needed for the underlying cause as guided by clinical evaluation, such as:

- Cardiac enzyme and creatine kinase (CK)
- Urine toxicology screen for suspected substance use
- Inflammatory markers and test for autoimmune cause
- Specific serologies for: Lyme disease, Chagas disease

Echocardiography (confirmatory and investigation of choice)

- Left ventricular cavity size: Significantly increased (LV dilation)
- Left ventricular ejection fraction (LVEF): Significantly decreased
- Ventricular wall thickness: Normal or decreased
- Additional features: Systolic dysfunction, Normal diastolic function

Electrocardiography (ECG): To assess for complications and rule out tachycardia-induced cardiomyopathy, changes are common, they are non-specific – ST segment & T wave changes, conduction abnormalities (AV block, LBBB), Atrial fibrillation and other tachyarrhythmias.

Chest X-ray (CXR): Shows finding of congestive heart failure – cardiomegaly (left-sided enlargement) with a balloon appearance, pleural effusion, pulmonary edema and may show hilar lymphadenopathy in sarcoidosis.

Cardiac MRI: It is helpful in inflammatory or infiltrative disease, such as sarcoidosis or hemochromatosis, and is the diagnostic study of choice for RV dysplasia. MRI can also help define an ischemic etiology by noting gadolinium hyperenhancement consistent with myocardial scar from infarction or prior myocarditis

Genetic testing: it is indicated for suspected familial or idiopathic etiology.

Note: For below medication and its drug dosing see treatment of Congestive heart failure



TREATMENT OF DILATED CARDIOMYOPATHY (DCM)

- The focus of management is to control or treat congestive heart failure using the strategies explained in CHF.
- Patients with dilated cardiomyopathy and moderate or severe heart failure are at risk of sudden arrhythmic death and this can be reduced by rigorous medical therapy with beta-blockers and either ACE inhibitors or ARBs.
- Identification and treatment of the underlying etiology as mentioned above
- Encourage complete abstinence from alcohol, avoid cardiotoxic drugs and toxins, if possible.
- Provide supplemental oxygen via mask: indicated for patients with an $SpO_2 < 90\%$
- Vitals monitoring: B.P, P.R, R.R, Temperature, SpO_2 (pulse oximetry)
- Send initial labs: CBC, BUN, serum creatinine, serum electrolytes, LFTs, FBS, troponin-I level, Creatine kinase (CK), ESR, CRP, TSH level and NT-proBNP (or BNP). Obtain Chest x-ray, 12-lead ECG and arrange early echocardiography
- Standard therapy includes:
 - Systemic BP control is extremely important and of contributing factors such as obesity, smoking, diabetes inhibitors, ARBs, or sacubitril/valsartan. Beta-blockers should be included in this population as well.
 - All patients with DCM regardless of etiology should be treated with beta-blockers & ACE inhibitors. If still symptomatic, aldosterone antagonists should be added, & ARNI used instead of an ACE inhibitor or ARB.
 - The use of the combination of all three of ACE inhibition, ARB, and aldosterone antagonists can create harm, though, and is discouraged due to concerns for hyperkalemia.
 - CCBs should be avoided except as necessary to control ventricular response in atrial fibrillation or flutter.
 - If congestive symptoms are present aldosterone receptor antagonists (Spironolactone and eplerenone) should be added. In patients with class II-IV heart failure symptoms, an aldosterone receptor antagonist should be added when the LVEF is $< 35\%$ (unless contraindicated). Care in the use of Aldosterone receptor antagonists is warranted when the GFR is < 30 mL/minute/1.73 m² or when the potassium is elevated.
 - All patients with diabetes should be taking Aldosterone antagonists if the LVEF is less than or = 40%.
 - Use of the ARNI, sacubitril/valsartan, has been approved for NYHA Heart Failure of Functional class II-IV.
 - If the resting heart rate is > 70 beats/minute, the LVEF is $< 35\%$, and the patient has chronic stable heart failure the use of ivabradine to slow the heart rate has also been approved. Ivabradine should not replace other beta blockers, however. Digoxin is a second-line medication but remains favored as an adjunct by some clinicians.
 - Digoxin may be beneficial to reduce recurrent hospitalizations and to control the ventricular response in atrial fibrillation in sedentary patients. Given the question of abnormal nitric oxide utilization in Blacks, the use of hydralazine-nitrate combination therapy is recommended in this population.
 - Sodium restriction is helpful, especially in acute heart failure.
 - Continuous positive airway pressure can improve LV function in patients with sleep apnea.
- Management of complication: CHF, Atrial fibrillation, Thromboembolic events, secondary mitral regurgitation
- In severe or refractory disease, consider for: implantation of a cardiac defibrillator and/or cardiac resynchronization therapy, Left ventricular assist devices and Heart transplantation.

HYPERTROPHIC CARDIOMYOPATHY

Clinical definition: Hypertrophic cardiomyopathy characterized by ventricular hypertrophy and diastolic dysfunction. It is second most common cardiomyopathy. Non-obstructive hypertrophic cardiomyopathy (HCM) is one of the most frequent causes of sudden cardiac death in young patients, especially young athletes.

Types of Hypertrophic cardiomyopathy

- » **Non-obstructive hypertrophic cardiomyopathy (HCM) = 30%:** Hypertrophic cardiomyopathy without obstruction of the left ventricular outflow tract (LVOT)
- » **Hypertrophic obstructive cardiomyopathy (HOCM) = 70%:** Hypertrophic cardiomyopathy with left ventricular outflow tract obstruction (LVOTO) that is dynamic.

ETIOLOGY

- » **Familial 100% (most common)**
- » **Inheritance pattern** most commonly autosomal dominant with high degree of penetrance and variable expression.
- » Approximately 60%–70% of cases are caused by mutations affecting the thick or thin myofilament proteins (defect in >100 myocardial protein) of the sarcomeres (contractile components of the heart).
- » **There are three common groups of mutation with different phenotypes:**
 - » **Beta-myosin heavy-chain mutations:** associated with marked ventricular hypertrophy
 - » **Troponin mutations:** Associated with little, if any, hypertrophy but are characterised by marked myocardial fibre disarray, exercise-induced hypotension and a high risk of sudden death.
 - » **Myosin-binding protein-C mutations:** present late in life & are often associated with hypertension & arrhythmia.
- » **Association with left-ventricular hypertrophy include the following:**
 - » Chronic hypertension (most common cause of left ventricular hypertrophy) and Aortic stenosis
 - » Storage disorders: Fabry disease, Amyloidosis
 - » hereditary syndromes: Friedreich ataxia, Noonan syndrome

PATHOGENESIS

- » **Non-obstructive hypertrophic cardiomyopathy (HCM):**
 - » Increased LV wall thickness with septal predominance, no dilation of left ventricle.
 - » Myofibrillary disarray, interstitial fibrosis, and myocyte hypertrophy
 - » Concentric hypertrophy of the left ventricle (including the interventricular septum) → ↓ ventricular relaxation → ↓ diastolic filling and systolic output → ↓ Myocardial and peripheral perfusion
- » **Hypertrophic obstructive cardiomyopathy (HOCM):** Left ventricular outflow tract (LVOT) obstruction and mitral regurgitation caused by due to systolic anterior movement (SAM) of the mitral valve.
 - » The following factors can increase the degree of obstruction: ↑ LV contractility, ↓ preload, and ↓ afterload.
 - » Clinically exacerbating factors: 1. Physical exercise/stress, 2. Dehydration, 3. Pharmacologic provocation (diuretics, ACEIs/ARBs, Digoxin, Hydralazine), 4. Valsalva maneuver (strain phase)

CLINICAL FEATURES

- | | |
|---|---|
| <ul style="list-style-type: none"> » Symptoms: symptoms worsen with exercise, dehydration, and use of certain medications → Diuretics, hydralazine, ACEIs, ARBs and digoxin » Frequently asymptomatic (especially the non-obstructive hypertrophic cardiomyopathy) » Dyspnea on exertion » Angina/Chest pain, especially with physical exertion » Dizziness, lightheadedness, syncope » Palpitations, cardiac arrhythmias » Sudden cardiac death (particularly during or after intense physical activity) from ventricular arrhythmia | <ul style="list-style-type: none"> » Physical examination <ul style="list-style-type: none"> » Systolic ejection murmur (crescendo-decrescendo) » Possible holosystolic murmur from mitral regurgitation » S4 gallop/loud S4 (a sign of left ventricular hypertrophy) » Sustained apex beat » Paradoxical split of S2 » Bisferiens carotid pulse: LV outflow obstruction causes a sudden quick rise of the pulse followed by a slower longer rise (biphasic pulse). |
|---|---|

Diagnostic criteria

- » Both of following are required to make the diagnosis:
 - » Left ventricular non-dilated hypertrophy (usually ≥ 15 mm in adults)
 - » Absence of other cardiac or systemic diseases that could explain hypertrophy for example long-standing hypertension or aortic stenosis.

DIAGNOSTIC WORKUP

- » **Initial laboratory test:** CBC, LFTs, BUN/urea, serum creatinine, serum electrolytes and blood sugar level.
- » For suspected Heart failure: NT pro-BNP or BNP
- » **Echocardiography with Doppler**
 - » Non-obstructive hypertrophic cardiomyopathy (HCM)
 - » Left ventricular cavity size: Decreased

- Left ventricular wall thickness: Significantly increased (≥ 15 mm typically involving the septum, ≥ 30 mm associated with a high risk of sudden death).
- Left ventricular ejection fraction: normal
- Outflow tract abnormalities: Systolic anterior motion of the mitral valve, Mitral regurgitation
- Additional finding: Diastolic dysfunction, Systolic function typically normal
- Finding more specific to Hypertrophic obstructive cardiomyopathy (HOCM):
 - Asymmetrically thickened interventricular septum
 - Dynamic LVOT obstruction due to contact between the septum and mitral valve during systole.
 - LVOT pressure gradient ≥ 30 mm Hg.
- Electrocardiography (ECG): Detect left ventricular hypertrophy with a wide variety of often bizarre abnormalities including deep T-wave inversion. Exaggerated septal 'Q waves' inferolaterally may mimic MI.
- Chest X-ray (CXR): Often unimpressive
- Cardiac MRI is gold standard: Confirms the hypertrophy and contrast enhancement frequently reveals evidence scar at the junction the RV attachment to the interventricular septum.
- Cardiac catheterization confirms the diagnosis and defines the presence or absence CAD.
- Genetic testing: Can be performed and is helpful in screening relatives of affected individuals.



TREATMENT OF HYPERTROPHIC CARDIOMYOPATHY

- All patients of hypertrophic cardiomyopathy
 - Counsel regarding lifestyle changes:
 - Avoidance of dehydration
 - Maintaining a healthy body weight
 - Avoidance of excessive alcohol intake
 - Avoidance of strenuous exercise & situations that will likely cause Vasodilation – Environmental factors such as high temperatures.
 - Automated implantable cardioverter defibrillator (AICD): an AICD placement should be considered in patients with clinical risk factors for sudden cardiac death (SCD). **ABSOLUTE INDICATION OF AICD:** known prior history of ventricular fibrillation, sustained ventricular tachycardia, or cardiac arrest. **RELATIVE INDICATIONS:** Syncope of unknown cause, Family history of SCD in a first-degree relative, Left ventricular wall thickness ≥ 30 mm
 - Treat cardiovascular comorbidities.
- Asymptomatic patients: No pharmacological or invasive treatment is needed.
- Symptomatic patients: The goal of treatment is to alleviate the symptoms of HCM by slowing the heart rate
 - Recommended pharmacological treatment:
 - Initial therapy: for all symptomatic patients with obstructive or non-obstructive HCM
 - First-line = Beta blockers (Titrate to goal resting heart rate $< 60 - 65$ per minute)
 - Tab. Propranolol 10mg, or 40mg (Inderal) at dose 20 – 80mg per orally every 8-12 hours
 - OR Tab. Atenolol 25mg or 50mg or 100mg (Tenormin) at dose 25 – 150mg per orally x once daily
 - OR Tab. Nadolol 40mg or 80mg (Corgard) 40 – 80mg per orally x once or twice daily
 - Second line: Non-dihydropyridine CCBs – Consider in patients who do not tolerate or respond to BBs
 - Verapamil is preferred but should be avoided if there is hypotension or dyspnea at rest.
 - Tab. Verapamil 40mg or 80mg (Calan) at dose 40mg orally every 8hrs, titrated up to 480mg/day.
 - Diltiazem may be considered in patients with an intolerance or contraindications to verapamil.
 - Tab. Diltiazem 30mg or 60mg (Hibesser) at dose 60mg orally every 8hrs, titrated up to 460mg/day
 - Additional therapy: to consider adding to beta-blocker or CCB if symptoms are persistent
 - Obstructive HCM: Disopyramide 100mg (Mopacel) at dose 200-250mg x BD, titrated up to 400-600mg/day
 - Obstructive HCM, or non-obstructive HCM with LVEF $> 50\%$: Tab. Furosemide (Lasix) 20-40mg x OD
 - Medication to be avoid: The following are relative contraindications and may not apply to all patients, e.g., those with acute complications such as heart failure or atrial fibrillation
 - Medications to be avoided in LVOT obstruction: High-dose diuretics, Digoxin, Spironolactone, ACE inhibitors and ARBs, Dihydropyridine CCBs (Nifedipine), Vasodilators (Nitrates and PDE-5 inhibitors) and Positive inotropes (dopamine, dobutamine, norepinephrine)
 - Medication to be avoided in non-obstructive HCM: Digoxin (except in atrial fib. with an LVEF $\leq 50\%$)
 - Consider invasive treatment for symptoms refractory to medical therapy:
 - Septal reduction therapy: Surgical septal myectomy, Transcatheter ablation of septal hypertrophy
 - Dual-chamber pacemaker: Consider for patients who are poor candidates for septal reduction therapy
 - Heart transplant: Consider in end-stage non-obstructive HCM when LVEF $\leq 50\%$.
 - Manage complications: Shock, Atrial fibrillation, congestive heart failure (CHF) and ventricular arrhythmias

RISK FACTORS FOR SUDDEN CARDIAC DEATH (SCD) IN HYPERTROPHIC CARDIOMYOPATHY

- A history of previous cardiac arrest or sustained ventricular tachycardia
- Patient with recurrent syncope
- An adverse genotype &/or family history
- Exercise-induced hypotension
- Non-sustained ventricular tachycardia on ambulatory ECG monitoring
- Marked $\uparrow$ in left ventricular wall thickness

RESTRICTIVE CARDIOMYOPATHY (RCM)

Definition: Restrictive cardiomyopathy is characterized by impaired diastolic filling because the ventricles are 'stiff' with reasonably preserved LV chamber size. This leads to high atrial pressures with atrial hypertrophy, dilatation & later, AF.

ETIOLOGY

- Mostly idiopathic: may be sporadic or familial
- Systemic disorders: Amyloidosis (most common), Sarcoidosis, Hemochromatosis, Systemic sclerosis
- Primary hyperoxaluria: secondary to oxalate deposits in the myocardium
- Heart disease: Löffler endocarditis (eosinophilic infiltration of the myocardium), Endocardial fibroelastosis (diffuse thickening of the left ventricle endocardium from the proliferation of fibrous and elastic tissue)
- Post-radiation fibrosis and Drugs (anthracyclines)
- Iron overload: increased systemic iron from repeated blood transfusions
- Lysosome storage diseases: Anderson-Fabry disease, Mucopolysaccharidosis type-I and Gaucher disease
- Glycogen storage disorders: Niemann-Pick
- Malignancy: carcinoid heart disease or metastatic tumor

PATHOGENESIS

- Infiltration (e.g., abnormal proteins, glycogen, eosinophils, granulomas, iron) or Proliferation of connective tissue → ↓ Elasticity of cardiac tissue → Atrial enlargement and severe diastolic dysfunction

CLINICAL FEATURES

- Restrictive cardiomyopathy must be distinguished from constrictive pericarditis
 - The key feature is that ventricular interaction is accentuated with respiration in constrictive pericarditis and that interaction is absent in restrictive cardiomyopathy.
 - In addition, the pulmonary arterial pressure is invariably elevated in restrictive cardiomyopathy due to the high PCWP and is normal in uncomplicated constrictive pericarditis.
- Symptoms: Dyspnea on exertion (most common), ankle/sacral edema, palpitation, productive cough, dizziness, syncope, faintness, fatigue, sudden cardiac death (SCD).
- Physical examination
 - Right-sided heart failure: Jugular venous distention, Peripheral edema, Hepatomegaly, ascites & Kussmaul sign.
 - Auscultation:
 - Prominent S4 gallop (loud S4) and Possible murmur of Mitral Regurgitation and/or Tricuspid regurgitation
 - Possible dysrhythmia: Atrial fibrillation is common.
 - Signs of heart failure: Crackles or dullness 2° to pleural effusion
 - Features of the underlying disease:
 - Amyloidosis: carpal tunnel syndrome, Large tongue
 - Hemochromatosis: Bronze skin
 - Sarcoidosis: Erythema nodosum

DIAGNOSTIC WORKUP

- Electrocardiography (ECG): Low voltage QRS complexes, Conduction disorders (AV block, LBBB, RBBB) & A-fib.
- X-ray chest (PA and lateral view): Left atrial enlargement, pulmonary congestion and may show evidence of underlying disease (e.g. hilar adenopathy in sarcoidosis).
- Laboratory test
 - CBC with peripheral smear: Eosinophil count $> 1.5 \times 10^9/L$ is consistent with hypereosinophilic heart disease.
 - RFT, LFT, BUN & creatinine: Nephropathy and hepatopathy are common in amyloidosis.
 - Troponin & NT-proBNP: to establish the extent of heart failure and establish a baseline for treatment monitoring
 - 24 hr urine total protein
 - Iron profile: serum iron, total iron-binding capacity and ferritin levels in hemochromatosis
 - Angiotensin converting enzyme (ACE) level: increase in sarcoidosis
- Transthoracic echocardiography (TTE) is the preferred initial test.
 - Severe diastolic dysfunction (high early diastolic filling velocities and low late diastolic filling velocities)
 - Normal right and left ventricular volumes
 - Preserved EF (may be reduced in late-stage disease)
 - Typically normal ventricular wall thickness (may be ↑ in amyloidosis, sarcoidosis & lysosomal storage disease)
 - Left atrial or biatrial enlargement
 - Findings of underlying disease: Amyloidosis (reflective myocardium 'speckling'), sarcoidosis (regional wall motion abnormalities that do not match coronary blood flow distribution)
- Cardiac catheterization: used to assess for ischemic heart disease or constrictive pericarditis
- Cardiac MRI with a higher spatial resolution and late gadolinium enhancement (LGE): provide detail information.
 - Best to differentiate between constrictive pericarditis and restrictive cardiomyopathy (RCM) → If pericardial thickness is > 5 mm constrictive pericarditis, If pericardial thickness is normal (< 5 mm) in RCM.



TREATMENT OF RESTRICTIVE CARDIOMYOPATHY (RCM)



- » **Treatment of CHF:** Initial treatment of RCM is the treatment of congestive heart failure (CHF) – see above

 - » **Diuretics:** First-line treatment for heart failure secondary to restrictive cardiomyopathy (RCM)
 - » Tab. Furosemide 20mg or 40mg (Lasix) at starting dose 20–40 mg, usual dose 40–240 mg
 - OR Tab. Hydrochlorothiazide 25mg (Diuza) at starting dose 25 mg, usual dose 12.5–100 mg
 - OR Tab. Spironolactone 25mg (Aldactone) at dose 25mg/day x OD titrated to 50mg/day x OD
 - » **Beta blockers and CCBs:** reduced sympathetic tone, decreases arrhythmias, increase diastolic filling time
 - » Tab. Verapamil 40mg OR 80mg (Calan) at dose 40mg orally every 8hrs, titrated up to 480mg/day
 - » **ACEIs and ARBs:** Reduce afterload, Reduce ventricular hypertrophy
- » **Treatment of atrial fibrillation**

 - » **Early cardioversion:** Tachycardia can precipitate acute heart failure and hypotension.
 - » **Pharmacotherapy:**
 - » Consider = Tab. Sotalol 80mg (Betapace) OR Tab. Amiodarone 100mg or 200mg (Cordarone)
 - » Digoxin should be avoided in patients with RCM because it can worsen symptoms of several of the underlying etiologies (amyloidosis, sarcoidosis) and precipitate arrhythmia.
- » **Management of other type of arrhythmia:**

 - » Consider the following, depending on ECG and Holter monitor findings:
 - » **Pacemaker placement:** Patients with RCM frequently develop high-grade symptomatic AV blocks.
 - » **AICD:** Patients with RCM are at high risk for sudden cardiac death from ventricular dysrhythmias.
- » **Anticoagulation:**

 - » It is indicated for patients with a known thrombus, a high risk of thrombogenesis, or A-fib
 - » Atrial thrombi are not uncommon, although the role anticoagulation in amyloidosis remains ill defined.
- » **Disease-specific treatment:** Definitive treatment depends on the specific etiology

 - » **Light chain (AL) Amyloidosis:** Alkylator-based chemotherapy or high-dose melphalan followed by Autologous stem cell transplant
 - » **Immunoglobulin light chain Amyloidosis:** Standard or high chemotherapy, Autologous stem cell transplant, monoclonal antibodies and against plasma cells (Daratumumab)
 - » **Transthyretin (ATTR) Amyloidosis:** Liver transplant, Transthyretin stabilizers (Tafamidis), RNA antisense therapies (inotersen, patisiran), Monoclonal antibodies and Doxycycline with tauroursodeoxycholic acid
 - » **Sarcoidosis:** Immunosuppressive therapy, Pacemaker with or without AICD
 - » **Hereditary hemochromatosis:** Frequent phlebotomy, Iron chelation therapy (Deferoxamine)
 - » **Iron overload:** Iron chelation therapy (Deferoxamine)
 - » **Hypereosinophilic syndrome:** Corticosteroids, IFN- α , Hydroxyurea
 - » **Radiotherapy induced:** Symptomatic treatment, Possible heart transplant
 - » **Systemic sclerosis:** Symptomatic treatment, Early treatment with dihydropyridine CCB
- » **Management of severe or refractory restrictive cardiomyopathy (RCM)**

 - » In patients who are unresponsive to medical therapy, consider mechanical circulatory support (e.g., LVAD) either as a destination therapy or a bridge to transplant.
 - » Consider referral for a heart transplant OR heart and liver transplant in amyloidosis.
 - » For patients who are not candidates for a heart transplant, refer to palliative care

COMMONLY USED MEDICATIONS IN CARDIOVASCULAR DISEASES

GENERIC	BRAND NAME	ORAL DOSAGE
Beta blockers		
Atenolol	» Tab. Tenormin 25mg 50mg and 100mg » Tab. Normitab 25mg, 50mg and 100mg	Initial: 25 mg once daily Range: 25–100 mg in 1 or 2 doses
Metoprolol	» Tab. Mepressor 50mg, 100mg » Tab. Merol 25mg, 50mg, 100mg	Initial: 50 mg twice daily Range: 50–200 mg twice daily
Propranolol	» Tab. Inderal 10mg 40mg » Tab. Cardinal 10mg, 40mg	Initial: 20 mg twice daily Range: 40–320 mg in 2 doses
Nebivolol	» Tab. Nebilol 2.5mg, 5mg and 10mg » Tab. Nebil 2.5mg, 5mg and 10mg » Tab. Byscard 2.5mg, 5mg and 10mg	Initial: 5 mg once daily Range: 40 mg once daily
Bisoprolol	» Tab. Concor 2.5mg, 5mg and 10mg » Tab. Bispa 2.5mg, 5mg and 10mg	Initial: 2.5–5 mg once daily Range: 5–20 mg once daily
Carvedilol	» Tab. Dilatrend 6.25mg, 12.5mg and 25mg » Tab. Carvida 6.25mg, 12.5mg and 25mg » Tab. Carlov 6.25mg, 12.5mg and 25mg	Initial: 6.25 mg twice daily Range: 12.5–25 mg twice daily
Labetolol	» Tab. Labetolol 100mg	Initial: 100 mg twice daily Range: 200–2400 mg in 2 doses
Nadolol	» Tab. Cogard 20mg » Tab. Cogard 40mg	Initial: 20 mg once daily Range: 20–320 mg once daily
Pindolol	» Tab. Visken 5mg	Initial: 5 mg twice daily Range: 10–60 mg in 2 doses
Dihydropyridines – calcium channel blockers (CCBs)		
Amlodipine	» Tab. Norvasc 5mg, 10mg » Tab. Sofvasc 5mg, 10mg » Tab. Lodopin 2.5mg, 5mg, 10mg	Initial: 2.5 mg once daily Range: 2.5–10 mg once daily
Nifedipine	» Tab. Adalat retard 20mg » Tab. Adalat LA 30mg » Tab. Adalat LA 60mg » Tab. Adalat CR 60mg	Initial: 30 or 60 mg ER once daily Range: 30–120 mg ER once daily
Felodipine	» Tab. Plendil 5mg » Tab. Plendil 10mg	Initial: 5 mg ER once daily Range: 5–10 mg ER once daily
Nimodipine	» Tab. Bredin 30mg » Tab. Nimoden 30mg	Initially at dose 30mg to 60mg every 4–6 hours. Indicated in SAH
Non-Dihydropyridines – calcium channel blockers (CCBs)		
Diltiazem	» Tab. Herbesser 30mg, 60mg » Tab. Herbesser SR (90mg) » Tab. Etizem 30mg, 60mg » Tab. Dilzem 30mg, 60mg	Initial: 30mg QID, 60mg TDS OR 90 mg (SR) twice daily Range: 180–360 mg SR in 2 doses
Verapamil	» Tab. Calan 40mg, 80mg » Tab. Calan SR 240mg	Initial: 40mg TDS, 240mg x OD Range: 120–480mg TDS
Angiotensin converting enzyme inhibitors (ACEIs)		
Captopril	» Tab. Capoten 25mg	Initial: 6.25–25 mg 2–3 times daily Range: 50–150 mg in 2 or 3 doses
Enalapril	» Tab. Capoten 50mg » Tab. Renitec 5mg	Initial: 5 mg once daily Range: 5–40 mg in 1 or 2 doses
Ramipril	» Tab. Renitec 10mg » Tab. Tritace 1.25mg, 2.5mg, 5mg and 10mg	Initial: 2.5 mg once daily Range: 2.5–20 mg in 1 or 2 doses
Perindopril	» Tab. Ramipace 1.25mg, 2.5mg, 5mg & 10mg » Tab. Coversyl 2mg » Tab. Coversyl 2mg and 8mg	Initial: 4 mg once daily Range: 4–16 mg once daily
Lisinopril	» Tab. Zestril 5mg, 10mg, 20mg » Tab. Novatec 5mg, 10mg » Tab. Trupril 5mg, 10mg	Initial: 5–10 mg once daily Range: 5–40 mg once daily



Angiotensin receptor blockers (ARBs)		
Losartan	» Tab. Eziday 50mg, 100mg	Initial: 50 mg once daily (OD) Range: 50mg–100mg OD
	» Tab. Sartan 50mg, 100mg	Initial: 80 mg once daily Range: 80–320 mg once daily
Valsartan	» Tab. Diovan 80mg, 160mg	Initial: 8 mg once daily Range: 8–32 mg once daily
	» Tab. Nobel 80mg, 160mg	
Candesartan	» Tab. Advant 8mg and 16mg	
	» Tab. Cansaar 8mg and 16mg	Initial: 20–40 mg once daily Range: 20–80 mg once daily
Telmisartan	» Tab. Carac 8mg and 16mg	
	» Tab. Telsan 20mg, 40mg, and 80mg	
Olmesartan	» Tab. Tasmi 20mg, 40mg, and 80mg	
	» Tab. Telsarta 20mg, 40mg, and 80mg	Initial: 20 mg once daily Range: 20–40 mg once daily
Irbesartan	» Tab. Omsana 10mg, 20mg, 40mg	
	» Tab. Olesta 20mg, 40mg	
Irbesartan	» Tab. Beritec 20mg, 40mg	
	» Tab. IreCon 150mg, Tab. IreCon 300mg	Initial: 150 mg once daily Range: 150–300 mg once daily
Irbesartan	» Tab. Aprovel 150mg, Tab. Aprovel 300mg	
	» Tab. Arbi 150mg, Tab. Arbi 300mg	
Thiazides & related Diuretics		
Hydrochlorothiazide (HCTZ)	» Tab. Diuza 25mg	Initial: 12.5 or 25 mg once daily Range: 12.5–50 mg once daily
Indapamide	» Tab. Natrilix 2.5mg	Initial: 2.5 mg once daily
	» Tab. Natrilix 1.5 mg (SR)	Range: 2.5–5 mg once daily
Metolazone	» Tab. Metxone 5mg	Initial: 2.5–5 mg once daily
	» Tab. Metenix 5mg	Range: 1.25–20 mg x OD or BD
Loop Diuretics		
Furosemide	» Tab. Lasix 20mg	Initial: 20 mg twice daily
Ethacrynic acid	» Tab. Lasix 40mg	Range: 40–320 mg in 2 or 3 doses
	» Tab. Ethacrynic acid 25mg	Initial: 25–50 mg once daily (OD) Range: 50–400 mg OD or BD
Aldosterone receptor blockers		
Spironolactone	» Tab. Aldactone-A 25mg	Initial: 12.5 or 25 mg once daily
Eplerenone	» Tab. Aldactone 100mg	Range: 12.5–100 mg once daily
	» Tab. Epliron 25mg and 50mg	Initial: 25 mg once daily
	» Tab. Epler 25mg and 50mg	Range: 25–100 mg once daily
Alpha Blockers		
Prazosin	» Tab. Minipress 1mg	Initial: 1 mg 2 or 3 times daily;
Terazosin	» Tab. Minipress 2mg	take first dose at bedtime
	» Tab. Hytrin 1mg	Range: 2–20 mg in 2 or 3 doses
Doxazosin	» Tab. Hytrin 2mg	Initial: 1 mg at bedtime
	» Tab. Hytrin 5mg	Range: 1–20 mg in 1 or 2 doses
	» Tab. Cardura 2mg	Initial: 1 mg at bedtime Range: 1–16 mg once daily
	» Tab. Cardura 4mg	
Central Sympatholytics		
Clonidine	» Tab. Catapresan 0.15mg	Initial: 0.1 mg twice daily
Methyldopa	» Tab. Aldomet 250mg	Range: 0.2–0.6 mg in 2 doses
		Initial: 250mg 2 or 3 times daily Range: 500–3000 mg in 2 doses
Direct Vasodilators		
Hydralazine	» Tab. Hydralazine 25mg	Initial: 10 mg four times daily Range: 50–300 mg in 2–4 doses
Combination anti-hypertensive therapies (Once daily dosing as per above dosages)		
Enalapril 10mg + Hydrochlorothiazide 12.5mg	» Tab. Co-Renitec	
Lisinopril 20mg + Hydrochlorothiazide 12.5mg	» Tab. Co-Zeal, Tab. Zepres plus	
	» Tab. Zestoretic	
	» Tab. Co-trupril	
	» Tab. Coversam 4mg/5mg, 4mg/10mg, 8mg/5mg and 8/10mg	

Perindopril + Amlodipine	» Tab. Amlod-P 4/5mg, 8/5mg and 8/10mg
Perindopril 2mg + Indapamide 0.625mg	» Tab. Preterex
Perindopril 4mg + Indapamide 1.25mg	» Tab. Coversyl plus
Indapamide 1.5mg + Amlodipine	» Tab. Natrilam 1.5mg/5mg, Tab. Natrilam 10mg
Perindopril + Indapamide + Amlodipine	Perindopril 5mg or 10 + Indapamide 1.25mg or 2.5 + Amlodipine 5mg or 10mg
	» Tab. Triplixam 5/1.25/5mg
	» Tab. Triplixam 5/1.25/10mg
	» Tab. Triplixam 10/2.5/5mg
	» Tab. Triplixam 10/2.5/10mg
Atenolol 50mg + Chlorthalidone 12.5mg	Tab. Tenoret 50mg, Tab. Cardiolite 50mg, Tab. Blokium DIU 50mg
Atenolol 50mg + Chlorthalidone 25mg	Tab. Blokium DIU 100mg, Tab. Cardiolite 100mg
Losartan + Hydro-chlorothiazide	» Tab. Co-Eziday 50mg/12.5
	» Tab. Co-Eziday 100mg/25mg
Amlodipine + Valsartan	» Tab. Exforge 5/80mg
	» Tab. Exforge 5/160mg
	» Tab. Exforge 10/160mg
	» Other Brands: Tab. Avsar, Tab. Extor, Tab. Newday, Tab. Covance
Sacubitril + Valsartan	» Tab. Sacvin-50 = 24/26mg (50mg)
	» Tab. Sacvin-100 = 49/51mg (100mg)
	» Tab. Sacvin-200 = 97/103mg (200mg)
	» Other Brands: Tab. Savesto, Tab. Valsatril, Tab. Valsar-S, Tab. Uperio
Valsartan + Hydrochlorothiazide	» Tab. Co-Diovan 80mg/12.5, 160mg/12.5mg and 160mg/25mg
	» Tab. Exval-H 12.5, 160mg/12.5mg and 160mg/25mg
Amlodipine + Valsartan + Hydro-chlorothiazide	» Tab. Exforge-HCT 5+160+12.5mg
	» Tab. Exforge-HCT 10+160+12.5mg
	» Tab. Exforge-HCT 5+160+25mg
	» Tab. Exforge-HCT 10+160+25mg
	» Tab. Exforge-HCT 10+320+25mg
	» Other Brands: Tab. Avsar Plus, Tab. Co-Extor, Tab. Sofvasc-HCT
Telmisartan + Hydrochlorothiazide	» Tab. Co-Tasmi 40/12.5mg
	» Tab. Co-Telsan 40/12.5mg
	» Tab. Telsarta-D 40/12.5mg
Amlodipine + Telmisartan	» Tab. Am-Telsan 5/40mg
	» Tab. Am-Telsan 10/40mg
	» Tab. Mesar-AM 5/40mg
	» Tab. Mesar-AM 10/40mg
	» Tab. Telsarta-A 5/40mg
	» Tab. Telsarta-A 10/40mg
Amlodipine + Olmesartan	» Tab. Omsana 5/20mg, Tab. Omsana 10/40mg,
	» Tab. Olesta-AM 5/20mg, Tab. Olesta-AM 10/40mg
Olmesartan + Hydrochlorothiazide	» Tab. Omsana MIU 20/12.5mg, Tab. Omsana MIU 40/12.5mg
	» Tab. Co-Olesta 20/12.5mg, Tab. Co-Olesta 40/12.5mg
	» Tab. Co-Beritec 20/12.5mg, Tab. Co-Beritec 40/12.5mg
Amlodipine + Olmesartan + Hydrochlorothiazide	» Tab. Co-Olesta AM 20/5/12.5mg
	» Tab. Co-Olesta AM 40/5/25mg
	» Tab. Co-Olesta AM 40/10/25mg
Irbesartan + Hydrochlorothiazide	» Tab. Co-Aprovel 150mg/12.5mg
	» Tab. Co-Aprovel 300/12.5mg
	» Tab. Arbi-D 150/12.5mg
	» Tab. Arbi-D 300/12.5mg

Diuretics combinations

Furosemide 40mg + Amiloride 5mg	» Tab. Lasoride, Tab. Duride
Amiloride + Hydrochlorothiazide	» Tab. Moduretic (Amiloride 5mg + Hydro-chlorothiazide 50mg)
Triamterene + Hydrochlorothiazide	» Tab. Dyazide (Triamterene 50mg + Hydro-chlorothiazide 25mg)
Furosemide 20mg Spironolactone 50mg	» Tab. Spiromide 20
Furosemide 40mg Spironolactone 50mg	» Tab. Spiromide 40





MANAGEMENT NAUSEA &/OR VOMITING

- Gastrointestinal mucosal inflammation: Gastritis, GERD, Peptic ulcer disease (PUD)
- Gastrointestinal Infections: Acute gastroenteritis, Food poisoning
- CNS disorder: Migraine, Motion sickness, Benign paroxysmal episodic vertigo, Stroke (Ischemic, hemorrhagic)
- Metabolic and endocrine: Hypercalcemia, Hypothyroidism
- Mechanical gastrointestinal (GI) obstruction/Manipulation: Gastric outlet obstruction, small bowel obstruction, colonic obstruction, choledocholithiasis, cholecystitis
- Gastrointestinal (GI) pseudo-obstruction: Severe constipation, irritable bowel syndrome (IBS)

△ Nausea &/or vomiting

C/C:

Red flags for nausea and vomiting

- Abdominal
 - » Persistent vomiting
 - » Hematemesis
 - » Feculent vomiting
 - » Melena
 - » Hematochezia
 - » Acute and/or severe abdominal pain
 - » Progressive dysphagia
 - » Unintentional weight loss
- Neurologic
 - » Altered mental status
 - » Focal neurological deficit
 - » Meningeal signs
- Pulmonary/cardiovascular
 - » Dyspnea
 - » Chest tightness
 - » Feeling of impending doom

IMMEDIATELY LIFE-THREATENING CAUSES

- Hemorrhagic stroke
- CNS infection: Meningitis, Encephalitis
- Myocardial infarction
- Acute pancreatitis
- Bowel obstruction
- Bowel perforation
- Diabetic ketoacidosis (DKA)
- Adrenal crisis
- Drug overdose/withdrawal
- Poisoning (ingestion of toxins)

Diagnostic workup

- Routine Investigation: CBC, ESR, glucose, BUN, creatinine, electrolytes, LFTs, Pregnancy test (Beta-HCG urine/serum test)
- In patients with severe and sustained vomiting: ABGs and Urine ketones.
- Specific Ultrasound & X-Ray according to localization of symptoms
- Further diagnostic testing to consider based on localization of symptoms



Inpatient Treatment

- Stabilize patient with ABCD&E survey
- Establish intravenous (IV) access
- Keep patient NPO & Consider NPO diet.
- A nasogastric (NG) suction tube for gastric or mechanical small bowel obstruction improves patient comfort and permits monitoring of fluid loss.
- Perform screening examination and targeted diagnostics to rule out life-threatening & other causes (see below table).
- Once life-threatening causes have been ruled out:
 - » Conduct a detailed patient history and clinical examination.
 - » Consider further diagnostic testing.
- Identify and treat hypovolemia: Inj. 0.9% Normal saline
- Identify & treat electrolyte imbalance: I.V 0.45% NS with 20 mEq/L of potassium chloride is given in most cases to maintain hydration.
- Investigate, identify and treat the underlying cause.
- Minimize or discontinue any contributing medications.
- Administer ONE of the following antiemetic therapy:
 - ↳ Inj. Metoclopramide 10mg/2ml (Metacloclon) x IV/IM x TDS/QID
 - ↳ Inj. Dimenhydrinate 50mg/ml (Gravinate) x IV/IM x TDS/QID
 - ↳ Inj. Ondansetron 8mg/4ml (Onset, Onseron) x diluted in 50-100ml 0.9% NS over 15 minutes.
- Consider adjunctive corticosteroids if not controlled
 - ↳ Inj. Dexamethasone 4mg/ml (Decadron) at dose 4-8mg x IV



Outpatient (OPD) Treatment

- General measure: Most causes of acute vomiting are mild, self-limited, and require no specific treatment. Patients should ingest clear liquids (broths, tea, soups, carbonated beverages) and small quantities of dry foods (soda crackers). Ginger may be an effective non-pharmacologic treatment.
- Pharmacological treatment ANY of the following:
 - ↳ Tab. Metoclopramide 10mg (Metacloclon, Maxolon)
 - ↳ OR Tab. Dimenhydrinate 50mg (Gravinate) x TDS
 - ↳ OR Tab. Prochlorperazine 10mg (Stemetil) x TDS
 - ↳ OR Tab. Domperidone 10mg (Motilium, Domel) x TDS
 - ↳ OR Tab. Ondansetron 4mg (Onset, Onseron) x BD

LIFE-THREATENING CAUSES OF NAUSEA & VOMITING

Disease	Clinical features	Diagnostic findings
Acute coronary syndrome	» Heavy, dull, pressure/squeezing sensation » Substernal pain, radiate to left shoulder » Nausea, vomiting » Diaphoresis, anxiety » Dizziness, lightheadedness, syncope » Pain may improve with nitroglycerin	» ECG: nonspecific changes, ST-segment elevation/depression, T-wave inversions, pathological Q waves (old MI) » Increased or normal troponin » Echocardiography: hypokinesis, regional wall motion abnormalities
Acute pancreatitis	» Severe epigastric pain that radiates to the back » Nausea, vomiting » Epigastric tenderness, guarding, rigidity » Upper abdominal pain » Hypoactive bowel sounds » History of gallstones or alcohol use	» Increased Lipase, amylase » Abdominal ultrasound: pancreatic edema, peripancreatic fluid, gallstones » Abdominal CT with IV contrast: pancreatic edema, peripancreatic fat stranding, gallstones
Mechanical bowel obstruction	» Colicky abdominal pain » Obstipation/bloating » Progressive nausea and vomiting (late finding) » Diffuse abdominal distention, tympanic abdomen, collapsed rectum on DRE » Tinkling bowel sounds » History of abdominal surgery	X-ray abdomen » Dilated bowel loops proximal to the obstruction » Rectal air shadow absent » Multiple air-fluid levels CT abdomen with IV and oral contrast » Similar findings as on x-ray » Transition point at site of obstruction
Diabetic Ketoacidosis (DKA)	» Polyuria, polydipsia » Nausea and vomiting » Signs of volume depletion » Altered mental status, coma	» Hyperglycemia » High anion gap metabolic acidosis » Ketonuria » Ketonemia
Meningitis	» Classic triad: fever, headache, and neck stiffness (nuchal rigidity) » Meningism (e.g., photophobia), Dull, diffuse (holocephalic) headache that worsens over hours/days » Nausea, vomiting » Seizures, Altered mental status	» CBC: ↑WBC, ↑ Procalcitonin (if bacterial) » CSF analysis – Bacterial: WBC ≥ 1000 cells/μL (predominantly neutrophils), elevated protein, low glucose, positive gram stain – Viral: WBC 10-500 cells/μL (predominantly lymphocytes), normal-elevated protein, normal glucose
Hyperemesis gravidarum	» Severe, persistent nausea and vomiting associated with pregnancy » Weight loss and dehydration	» Ketonuria » Electrolyte and acid-base abnormalities

OTHER CAUSES OF NAUSEA AND VOMITING

Postoperative nausea and vomiting (PONV)	» Nausea and/or vomiting within the first 24-48 hours of surgery	» Clinical diagnosis
Chemotherapy-induced nausea and vomiting (CINV)	» Nausea and/or vomiting related to recent chemotherapy	» Clinical diagnosis
Uncomplicated first-trimester nausea and vomiting	» Nausea and vomiting associated with early pregnancy » Presumptive signs of pregnancy	» Urine and serum beta hCG positive
Infectious gastroenteritis	» Fever, Nausea, vomiting » abdominal pain, diarrhea, blood in stool » Normal abdominal examination » Exposure history	» Abdominal or transvaginal ultrasound: gestational sac or embryo, fetal heartbeat » Clinical diagnosis » Stool analysis (Stool D/R): Fecal leukocytes
Migraine	» Unilateral headache with pulsating, boring/hammering pain » Nausea, vomiting » Hyperacusis » Photophobia, Phonophobia » Preceding aura	» Clinical diagnosis » CT scan/MRI: Typically, normal findings

RECURRENT APHTHOUS STOMATITIS (ORAL ULCER/CANKER SORE)

Definition: Recurrent aphthous stomatitis (RAS), also known as "canker sores," is an oral ulcerative condition refers to small, painful ulcers that can appear on the inside of the lips, cheeks, or soft palate; on the floor of the mouth; on the gingiva of the teeth; or on the tongue.

Etiology: The exact cause of aphthous stomatitis is not currently known; however, there are many factors that are thought to contribute, including a weakened immune system; emotional or psychological stress; certain foods, such as coffee, chocolate, cheese, nuts, & citrus fruits; trauma to the mouth; viral and bacterial infection; poor nutrition; & certain medications, such as aspirin, beta-blockers, chemotherapy medicines, penicillamine, sulfa drugs, & phenytoin.

△ Oral Ulcer/Aphthous stomatitis**C/C:**

- » Recurring, painful, solitary, or multiple ulcers, Swollen skin around the sores
- » Typically covered by a white to yellow pseudomembrane surrounded by an erythematous halo
- » Usually involves nonkeratinizing mucosa (e.g., labial mucosa, buccal mucosa, and ventral tongue)
- » Problems with chewing or tooth brushing because of the tenderness
- » Irritation of the sores by salty, spicy or sour foods
- » Unable to eat/drink
- » Stress/Anxiety

Three Clinical Forms

- » Minor (<7mm in diameter), most common – Appears as rounded, well-demarcated, single or multiple ulcers that usually heal in 10–14 days without scarring
- » Major (>7mm in diameter) – Usually take longer than 14 days to heal and may result in scarring
- » Herpetiform

Duration of Treatment: Typically, aphthous ulcers heal within 7–14 days and leave no scar. Aphthous ulcers are generally non-serious and will go away without any particular treatment.

Rx

- » Most mild aphthous require no treatment.
- » Avoiding trigger foods can help reduce recurrences.
- » Celiac disease should be considered in patients with recurrent aphthous ulcers or stomatitis.

1. Topical anesthetic/anti-septic pain-relieving gel:

- » **Choline Salicylate + Cetalkonium Chloride** (Bonjela gel)
 - OR **Lignocaine + Cetylpyridinium Chloride + Ethanol** (Somogel)
 - OR **Dequalinium Chloride** (Solophar Spray)
 - OR **Benzylamine + Cetylpyridinium** (Enziclor gel, Dentisept gel) (ThroatSil Mouth Spray)
 - OR **Benzocaine + Amylmetacresol + 2, 4 Dichlorobenzyl Alcohol**
- Apply on affected area/oral sores every 4–6 hours, retain for 20–30 second then spit.

2. Anti-inflammatory agents:

- » **Triamcinolone oral emollient** (Kanaolog in orabase)
 - OR **Dexamethasone elixir**
- Topical application on oral sores 2–3 time a day after meal and taking care not to eat or drink during 20 minutes after application, or touch the treated zone, for 3–5 minutes. If the corticosteroid is given as an oral rinse, it should be used for the indicated period of time, without swallowing the product.

3. Anti-Infective

- » **Tab. Minocycline 100mg** (Minogen, Minoderm)
- OR **Cap Doxycycline 100mg** (Doxyn, Vibramycin)
- » **Recommend dose:** 100 mg in 10 ml of water, performing rinses for 2 to 3 minute (without swallowing), four times a day for 3 days.

4. Tab. Vitamin B-Complex (Neurobion, Bevidox) x 1–0–1 (BD)

Note: Minocycline and Doxycycline is contraindicated in < 8 years of age, in pregnancy, and lactation (discolors developing tooth enamel). Do not give with antacids, calcium supplements, milk or other dairy, or within 2 hours of taking another drug.



ORAL THRUSH (OROPHARYNGEAL CANDIDIASIS)

Name: _____ Age: _____ Sex: _____ Date: _____
 Temperature: _____ B.P: _____ Pulse: _____ Resp. Rate: _____

Definition: Oral thrush (oropharyngeal candidiasis/oral pseudomembranous candidiasis) causes curd-like white patches inside the mouth, on the tongue and palate and around the lips. It may also cause cracked, red, moist areas of skin at the corners of the mouth. Thrush patches may or may not be painful.

Etiology: Most commonly caused by candida albicans (C. Albicans)

Risk factors

- » **Immunosuppression is the main risk factor for infection:** HIV, Diabetes mellitus, Neutropenia & certain patient groups (e.g., ICU, transplant patients, surgical patients, and neonates)
- » **Imbalance in local flora:** (Medications - antibiotics, steroids, cytostatic agents, immunosuppressive therapy and ↑ Estrogen levels during pregnancy)

Clinical features

- » White plaque in the oral cavity that can be scraped off, giving way to red, inflamed, or bleeding areas.
- » Cottony feeling in the mouth, loss of taste, and in some cases pain while eating
- » Fissuring at the mouth corners

Diagnostic workup

- » **Diagnosis:** a suspected diagnosis based on clinical appearance requires confirmation and may be required additional tests.
- » **Best initial test:** KOH test (potassium hydroxide smear) on a wet mount preparation of scrapings or smears - Shows budding yeasts, hyphae, and pseudohyphae
- » **Best confirmatory test:** blood or tissue culture



Acute pseudomembranous candidiasis of the dorsum of the tongue.
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Oral pseudomembranous candidiasis infection.
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TREATMENT OF ORAL THRUSH

Rx

Practice good oral hygiene.

- » Brush teeth regularly.
- » Use warm saline water as a mouth wash.
- » Avoid use/overuse of antiseptic mouthwashes, as they alter the flora of the mouth.
- » If using a steroid inhaler for asthma, drink water and rinse mouth after inhalation.

Denture wearers:

- » Patients must clean and disinfect their dentures daily and remove them for at least six hours every night.
- » Clean dentures with an anti-candidal preparation, such as 1% sodium hypochlorite solution.
- » Remove dentures overnight.
- » **Mouthwashes with anti-candidal activity include:** Triclosan, Chlorhexidine gluconate

1. **Nystatin 100'000 units/ml drops** (Nilstat, Myconil)
Dosage: 400,000 to 600,000 units (4 to 6 mL) swish in mouth several minutes and then swallow x four times daily for 7 to 14 days

OR **Miconazole** (Daktarin oral gel, Macnaz oral gel)
Dosage: 2.5 ml after food 4 times daily.

- » **If treatment fails:** Oral fluconazole or Itraconazole
Cap. Fluconazole 150mg (Diflucan, Fluderm, Flucon)
Dosage: at dose 150 mg once daily, until symptoms of oropharyngeal candidiasis is clear, usually for 7–21 days

OR **Cap. Itraconazole 100mg** (Icon, Rolac, Sporanox)
Dosage: 200mg x OD (or 100 mg x BD) for 7–14 days
 Signs and symptoms of oropharyngeal candidiasis generally resolve within several days

2. **Vitamin-B complex** (Neurobion, Bevidox) x 1–0–1 (BD)



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GASTRO-ESOPHAGEAL REFLEX DISEASE (GERD)

Age:

Sex:

Date:

B.P.:

Pulse:

Resp. Rate:

Name:

Temperature:

GERD

C/C:

Typical symptoms

- » Retrosternal burning pain (heartburn) that worsen while lying down (at night/after eating)
- » Regurgitation
- » Dysphagia, odynophagia
- » Water brash: symptom of excessive salivation triggered by refluxing of stomach acid

Atypical symptoms

- » Pressure sensation in the chest
- » Non-cardiac chest pain
- » Belching, bloating
- » Dyspepsia, epigastric pain
- » Nausea, Halitosis

Extra-esophageal symptoms

- » Chronic non-productive cough and nighttime cough
- » Hoarseness
- » Dental erosions

Aggravating factors

- » Lying down shortly after meals
- » Certain foods/beverages

Duration of treatment: 6-8 weeks

Investigation:

1. Upper endoscopy: UGD → Age ≥60 years, atypical symptoms, or alarm features (Anemia dysphagia, odynophagia, Barret esophagus)
2. 24 hour Esophageal pH monitoring
3. Esophageal manometry

Treatment with PPIs:

Standard dose of PPI for 8 weeks.

- » Continuous management (based on the clinical response after 8 weeks)
 - Good response and no complications: Discontinue PPI.
 - Good response in patients with complications: Continue PPI at maintenance dose.
 - Partial response: Increase the dose (to twice daily therapy), adjust timing, or switch to a different PPI (Esomeprazole, Omeprazole).
 - Recurrence of symptoms after discontinuation of PPI (Esomeprazole, Omeprazole) or during weaning: Consider confirming the diagnosis (e.g., with ambulatory esophageal pH monitoring) prior to continuing maintenance therapy.
 - No response: further diagnostic evaluation
- » There is controversy surrounding the risks of long-term PPI therapy

Rx

TREATMENT OF GERD (FIRSTLINE)

1. Life-style modification

- » Dietary recommendations
 - » Small portions of foods.
 - » Avoid eating at least 3-4 hours before bedtime.
 - » Avoid triggers: Foods, peppermint, beverages.
- » Physical recommendations
 - » Weight loss in patients with obesity
 - » Elevate the head of the bed (10-20 cm) for patients with nighttime symptoms.
- » Reduce or avoid triggering substances
 - » Nicotine, alcohol, caffeine if the patient experiences a correlation with symptoms
 - » Drugs that may worsen symptoms: E.g., CCBs, Diazepam

2. Cap. Esomeprazole 20mg, 40mg (Nexum, Eso)
 - OR Cap. Dexlansoprazole 30mg, 60mg (Razodex, Desktop)
 - 1-0-1 (20mg/30mg = BD) OR 1-0-0 (30mg/40mg = OD)
 - کھانے سے 30 منٹ پہلے
 - 20mg BD, 40mg OD x 30 minutes before meals.

3. ± Tab. Metoclopramide 10mg (Metoclon, Maxolon)
 - 1-1-1 (TDS)
 - کھانے سے 30 منٹ پہلے

4. Consider adding: Antacids.
 - » Syp. Gaviscon Advance x 10ml (2 teaspoonful) x BD
 - » OR Syp. Mucain x 10ml (2 teaspoonful) x BD
 - » OR Syp. Mylanta-2 x 10ml (2 teaspoonful) x BD

Rx

TREATMENT OF GERD (SECOND LINE)

1. Life-style modification

2. Tab. Pantoprazole 40mg (Zopent, Protium)
 - OR Tab. Vonoprazan 20mg (Vonozan, Voniza)
 - 0-0-1 (OD) Once daily x 30 minutes before meals
 - کھانے سے 30 منٹ پہلے
3. Consider adjunctive prokinetic:
 - » Tab. Itopride 50mg (Ganaton, Nogerid)
 - » OR Tab. Levosulpride 25mg or 50mg (Sulvorid, Pride)
 - Two times a day (BD) x 30 minutes before meals
 - کھانے سے 30 منٹ پہلے

- ± In case of psychogenic dyspepsia/features of Depression
- 4. Cap. Fluoxetine 20mg (Flux, Depex)
- OR Tab. Escitalopram 5mg or 10mg (Estar, Citanew)
- ایک گولی صبح ناشتے کے بعد
- One tab after breakfast (OD)

STOMACH ULCER/PEPTIC ULCER (GASTRIC ULCER/ DUODENAL ULCER)

Name:
Temperature:

Age:
B.P:

Sex:
Pulse:

Date:
Resp. Rate:

△ Gastric Ulcer

C/C:

- » Pain: Epigastric Can radiate to back
- » Onset: Immediately after eating
- » Aggravated by: Eating
- » Relieved by: Lying down or vomiting
- » Duration: Few weeks
- » Vomiting: Common
- » Appetite: Patient afraid to eat
- » Weight loss: Yes

△ Duodenal Ulcer

C/C:

- » Pain: Epigastric, discomfort
- » Onset: 2-3 hours after eating & midnight
- » Aggravated by: Hunger
- » Relieved by: Eating
- » Duration: 1-2 months
- » Vomiting: Uncommon
- » Appetite: Good
- » Weight loss: Not

Duration of treatment: Recommended duration of acid suppression for Gastric ulcers is ≥8 weeks and for Duodenal ulcers: ≥4 weeks.

Peptic ulcer Unknown location: Consider 8 weeks of empiric treatment

Diagnostic workup: see H.pylori

- » CBC to rule out anemia
- » H. pylori stool Antigen, Urea breath test.
- » UGI Endoscopy (see detail below in H.Pylori)

PPIs (most effective)

- » Cap. Omeprazole 40mg (Ruling, Risek)
- » Cap. Esomeprazole 40mg (Esso, Nexum)
- » Tab. Pantoprazole 40mg (Zopent)
- » Cap. Lansoprazole 30mg (Selanz SR, Qpro)
- » Cap. Dexlansoprazole 30-60mg (Dolgina, Dextop)
- » Tab. Rabeprazole 20mg (Rabecid, Repar)

PPIS SIDE-EFFECTS (WITH LONG TERM USE)

- » Osteoporosis/fracture due to decrease absorption of calcium and magnesium
- » Increase risk of clostridium difficile infection
- » Decrease absorption of Iron (Iron deficiency) and B12 (Vitamin B12 deficiency)
- » Reactive Hypergastrinemia
- » Increase risk of pneumonia

Rx

Prescriptions #1

1. Cap. Omeprazole 20mg OR 40mg (Omezol, Risek, Ruling)
OR Cap. Esomeprazole 20mg or 40mg (Eskem, Nexum, Esop)
1-0-1 (20mg = BD) OR 1-0-0 (40mg = OD)
کھانے سے 30 منٹ پہلے
20mg BD, 40mg OD x 30 minutes before meals.
2. For functional dyspepsia/Heartburn/features of depression
» Tab. Cinitapride 1mg (Cidine, Cinita)
OR Tab. Levosulpride 25mg, 50mg (Levopraid, Sulvorid)
1-0-1 (BD) x 30 minutes before meals.
کھانے سے 30 منٹ پہلے

Rx

Prescriptions #2

1. Tab. Pantoprazole 20mg OR 40mg (Zopent, Zentro)
OR Cap. Dexlansoprazole 30mg or 60mg (Razodex, Dextop)
1-0-1 (BD), 0-0-1 (OD)
کھانے سے 30 منٹ پہلے
20mg BD, 40mg OD x 30 minutes before meals
2. Consider adding: Antacids.
» Syp. Gaviscon Advance x 10ml (2 teaspoonful) x BD
» OR Syp. Mucain x 10ml (2 teaspoonful) x BD
» OR Syp. Mylanta-2 x 10ml (2 teaspoonful) x BD
3. For functional dyspepsia/Heartburn/depression:
» Tab. Cinitapride 1mg (Cidine, Cinita)
OR Tab. Levosulpride 25mg OR 50mg (Pride, Sulvorid)
1-0-1 (BD) x 30 minutes before meals.
کھانے سے 30 منٹ پہلے

Rx

Prescriptions #3

1. Tab. Vonoprazan 10mg OR 20mg (Vonozan, Voniza, Vonnol)
1-0-1, (10mg = BD), 0-0-1 (20mg = OD)
2. For functional dyspepsia/Heartburn/depression
» Tab. Cinitapride 1mg (Cidine, Cinita)
OR Tab. Levosulpride 25mg OR 50mg (Levopraid, Pridel)
1-0-1 (BD) x 30 minutes before meals.
کھانے سے 30 منٹ پہلے

→ If peptic ulcer is severe or not respond to above treatment → Triple therapy for 14 days

HELICOBACTER PYLORI (H.PYLORI) INFECTION

MECHANISMS OF PHYSIOLOGICAL DISRUPTION OF H. PYLORI

- **Gastric ulcers:**
 - *Helicobacter pylori*: Secretes urease → conversion of urea to NH_3 → alkalinization of acidic environment → survival of bacteria in gastric lumen
 - Bacterial colonization and attachment to epithelial cells → release of cytotoxins (e.g., cagA toxin) → disruption of the mucosal barrier and damage to underlying cells
- **Duodenal ulcers:**
 - *Helicobacter pylori*: Inhibits somatostatin secretion → Increased gastrin secretion → Increased hydrogen (H^+) secretion → excess hydrogen (H^+) delivery to the duodenum
 - Direct spread of *H. pylori* to the duodenum → inhibition of duodenal HCO_3^- secretion → acidification and insufficient neutralization of duodenal contents

DIAGNOSTIC APPROACH FOR SUSPECTED PUD/H.PYLORI

- **Initial evaluation for all patient group**
 - Screen for common etiologies on history, e.g., NSAID use, smoking, steroids, caffeine, alcohol, diet
 - Consider the following investigation if there is suspicion for occult bleeding: CBC, BUN/Urea, creatinine, stool occult blood test
 - Patients ≤ 60 years of age without red flags for dyspepsia
 - **Begin with noninvasive testing for *H. pylori* infection:** A positive result indicates exposure to *H. pylori*, but cannot distinguish between a past and current infection. Antibodies may still be detected after eradication.
 - **Urea breath test:** Detects a labeled carbon isotope in a breath sample; Can be used for initial diagnosis or confirmation of eradication, Sensitivity increases if PPIs have been discontinued for at least 2 weeks prior to testing.
 - ***H. pylori* stool antigen test:** Can be used for initial diagnosis or confirmation of eradication
 - **Serum IgG antibodies against *H. pylori***
 - **Refer directly for EGD**
 - Patients > 60 years of age, or > 45 years of age in areas with high gastric cancer prevalence
 - **Patients with red flags for dyspepsia:** on a case-by-case basis
 - Patients unresponsive to *H. pylori* eradication therapy, PPI trial therapy
- **Further evaluation:**
 - All patients with persistently uncertain etiology → Consider secretin stimulation test for gastrinoma (specialized laboratory studies).
 - Esophagogastroduodenoscopy (EGD): **The most accurate test to confirm the diagnosis.**
 - Other clinical applications of EGD include:
 - **Malignancy screening:** to differentiate PUD from gastric cancer
 - Visualization of the lesions
 - Biopsy sampling
 - Invasive *H. pylori* testing
 - **Simultaneous therapeutic measures:** hemostasis treatment with Electrocautery for active bleeding

CLASSIC ENDOSCOPIC APPEARANCE OF PEPTIC ULCERS

	Benign	Malignant
Base	Smooth	Ulcerated mass protruding into the lumen
Edges	Rounded, regular	Irregular, overhanging
Surrounding mucosa	Regular	Nodular, irregular
Location	Gastric ulcers: lesser curvature of stomach, b/w the corpus and antrum Duodenal ulcers: anterior or posterior wall of the duodenal bulb	Atypical
Histopathology	Chronic inflammatory changes and active granulation	Dysplasia, invasion of deeper layers
• Gastrinoma:	multiple ulcers and thick gastric folds	

TREATMENT GUIDELINES FOR H. PYLORI ASSOCIATED ULCER (H. PYLORI ERADICATION THERAPY)

STANDARD BISMUTH BASED QUADRUPLE THERAPY (14 DAYS)

Best option – Preferred in areas with high levels $\geq 15\%$ of clarithromycin resistance

Non-pharmacological management in H. Pylori

Dietary recommendations

- » Reduce portion size.
- » Avoid eating at least 3 hours before laying down (e.g., before going to sleep).
- » Avoid foods and beverages that appear to trigger symptoms. (dietary products, lussi, excessive intake of tea/coffee, heavy food like Paya, Liver/Kaliji, Paratha, Chole, which make patient uncomfortable)

Physical recommendations

- » Patients with obesity should be encouraged to lose weight & should also receive advice on the best approach
- » Elevate the head-end of the bed (10–20 cm) for patients who experience symptoms while sleeping.

Reduce or avoid triggers

- » Reduce or avoid stress.
- » Avoid nicotine, alcohol, and caffeine (especially if they appear to trigger symptoms).
- » If possible, avoid medications that may worsen symptoms: For example, NSAIDs, Aspirin, corticosteroids, calcium channel blockers (CCBs), Benzodiazepine (diazepam).

1. PPI: Cap. Omeprazole 20mg – 40mg (Ruling, Omezol) OR Cap. Esomeprazole 20mg – 40mg (Eskem, Esso) x Twice daily (1–0–1) x on empty stomach 30 minutes before meal (کھانے سے 30 منٹ پہلے)
2. Tab. Bismuth subsalicylate 265mg (Bismol) x Two tablets orally four times daily (2–2–2–2)
3. Cap. Tetracycline 500mg x One capsule orally four times (QID) daily (1–1–1–1)
4. Tab. Metronidazole 400mg (Klint, Metrozine, Flagyl) x Three time a day (1–1–1)

Rx

RIFABUTIN-BASED TRIPLE THERAPY (TALICIA)

1. PPI: Cap. Omeprazole 40mg (Ruling, Omezol) OR Cap. Esomeprazole 40mg (Eskem, Esso) x every 8 hour
 2. Tab. Rifabutin 50mg x every 8 hour (three times a day)
 3. Tab. Amoxicillin 1g (Zeemox, Ospomox) x BD OR Cap. Amoxicillin 500mg (Amoxil, Zeemox) x 2 capsule x BD
- OR Cap. Talicia x Four capsules three time a day, each capsule contains omeprazole 10 mg/rifabutin 12.5 mg/amoxicillin 250 mg, orally every 8 hours, thus total dosages are

Rx

VENOPRAZAN BASED TRIPLE THERAPY (14 DAYS)

1. Tab. Clarithromycin 500mg (Klaricid, Claritek, Ultima) x Twice daily (1–0–1)
2. Tab. Amoxicillin 1g (Zeemox, Ospomox) x BD OR Cap. Amoxicillin 500mg (Amoxil, Zeemox) x 2 capsule x BD
3. Tab. Vonoprazan 20mg (Vonozan, Voniza, Vociniti) x Twice daily (1–0–1)

Rx

VENOPRAZAN BASED DUAL THERAPY (14 DAYS)

1. Tab. Amoxicillin 1g (Zeemox, Ospomox) x TDS OR Cap. Amoxicillin 500mg (Amoxil, Zeemox) x 2 capsule x TDS
2. Tab. Vonoprazan 20mg (Vonozan, Voniza, Vociniti) x Twice daily (1–0–1)

Rx

STANDARD TRIPLE THERAPY (14 DAYS)

No longer recommended, except in locales where clarithromycin resistance is $< 15\%$

1. Tab. Clarithromycin 500mg (Klaricid, Claritek, Ultima) x Twice daily (1–0–1)
 2. Tab. Amoxicillin 1g (Zeemox, Ospomox) x BD OR Cap. Amoxicillin 500mg (Amoxil, Zeemox) x 2 capsule x BD
- OR Tab. Metronidazole 400mg (Klint, Metrozine, Flagyl) x Three times a day (1–1–1)
- PPIs: Cap. Omeprazole 20–40mg (Ruling, Omezol) OR Cap. Esomeprazole 20mg–40mg (Eskem, Esso) 1–0–1 (BD) Twice daily on empty stomach 30 minutes before meal (کھانے سے 30 منٹ پہلے)

H. PYLORI FOLLOW-UP TREATMENT (AFTER 14 DAYS)

- After completion of course of H. Pylori eradication therapy, continue treatment with PPI (Esomeprazole, Pantoprazole) x 40mg once daily for 4 – 6 weeks if ulcer is large (> 1cm) or complicated ulcer.
- Confirm successful eradication of H. pylori with urea breath test, stool antigen test, or PCR test or endoscopy with biopsy at least 4 weeks after completion of antibiotics treatment and 2 weeks after completion of PPI treatment
- Stop PPIs at least 2 weeks before the urea breath test is performed for accurate results.
- SEROLOGY IS NOT RECOMMENDED TO CONFIRM ERADICATION, AS H. PYLORI ANTIBODIES MAY STILL BE PRESENT FOR WEEKS OR MONTHS AFTER ERADICATION.**
- Acid suppression medication can be discontinued once eradication is confirmed.

FUNCTIONAL DYSPEPSIA

- Functional dyspepsia (nonulcer dyspepsia) is a common GI disorder characterized by upper GI symptoms (e.g., epigastric pain, bloating) without any identifiable cause.
- Symptoms may vary in intensity and can have a significant impact on patients' lives.
- Functional dyspepsia is heterogeneous and multifactorial, and its pathophysiology is not fully understood.

Rome IV criteria for functional dyspepsia

- Functional dyspepsia is a diagnosis of exclusion that can be made if an organic cause cannot be identified after completing a diagnostic workup of dyspepsia and its differential diagnoses.
- Any of the following symptoms experienced at least 3 days per week over the past 3 months:
 - Epigastric burning
 - Epigastric pain
 - Early satiety
 - Postprandial fullness

Rx

- First-line treatment:** PPIs for 8 weeks at standard dose
 - Tab. Pantoprazole 20mg or 40mg x OD (Zopent, Zentro)
 - OR Cap. Omeprazole 20mg or 40mg (Risek, Ruling)
 - I – 0 – I (20mg = BD) OR I – 0 – 0 (40mg = OD)
 - One capsule of 20mg x BD or 40mg x OD 30 minutes before meals x ایک گولی 20 ملی گرام دن میں دو بار یا 40 ملی گرام روزانہ ایک بار کھاتے سے 30 منٹ پہلے
- ±Second-line treatment (if no improvement after 8 weeks of PPIs)**
Add on TCAs (Amitriptyline) OR SSRIs (Fluoxetine)
 - Tab. Amitriptyline 25mg (Tryptanol, Amylin)
0 – 0 – I (OD), if needed titrated upto 50-150mg
OR Cap. Fluoxetine 20mg (Flux, Depex)
I – 0 – 0 (OD) x Once daily after breakfast
(ایک گولی دن میں ایک بار ناشتے کے بعد)
 - Cap. Esomeprazole 20mg or 40mg (Nexum, Esso)
I – 0 – I (20mg x BD), 0 – 0 – I (40mg x OD)
کھاتے سے 30 منٹ پہلے
- ±Third-line treatment:** Consider if there is no response to PPIs or tricyclic antidepressants (TCAs) PLUS add on → **Prokinetic therapy** (e.g., metoclopramide, Levosulpride, Cinitapride)
 - Tab. Levosulpride 25mg or 50mg (Sulvorid, Levopraid)
 - OR Tab. Cinitapride 1mg (Cidine, Cinita)
 - I – 0 – I (BD)
کھاتے سے 30 منٹ پہلے
 - OR Tab. Metoclopramide 10mg (Maxolon, Metoclon)
 - I – I – I (TDS)
کھاتے سے 30 منٹ پہلے
 - AND Psychological therapy (e.g., cognitive behavioral therapy)



CLOSTRIDIODES (CLOSTRIDIUM) DIFFICILE COLITIS

- Definition:** Clostridioides difficile infection (or Clostridium difficile infection), Also known as pseudomembranous colitis, CDI or CDAD. Caused by C. difficile bacteria. Characterized by inflammation of the colon and the formation of pseudomembranes. Occurs in patients whose normal bowel flora has been disrupted by recent antibiotic & PPIs use.
- Risk factors:** Recent antibiotic exposure (1. **High-risk antibiotics:** Cephalosporins, Clindamycin, Fluoroquinolones, Carbapenems, piperacillin-tazobactam. 2. **Moderate risk antibiotics:** Penicillin, Macrolides, tetracyclines, trimethoprim/sulfamethoxazole, Linezolid). Advanced age. Use of PPIs (E.g. Omeprazole, esomeprazole etc.), GI surgery or bypass (e.g. enteral feeding), Prolonged hospitalization, Immunosuppression agents, chemotherapy, Comorbidities (CKD, HIV, IBD) vitamin-D deficiency, solid organ transplant recipients and hematopoietic stem cells transplant patients.
- Classifications of Clostridioides difficile infection (CDI):**
- » **Community-onset-healthcare facility-associated CDI:** C. difficile infection (CDI) occurring within 7 weeks (28 days) after discharge from a healthcare facility.
 - » **Community-associated CDI:** C. difficile infection (CDI) in patients with no documented overnight stay in a healthcare facility in the prior 12 weeks.
 - » **Hospital associated CDI:** Laboratory-confirmed, C. difficile infection (CDI) in patients with documented inpatient care in a health care facility in the preceding 12 weeks.
 - » **Recurrent C. difficile infection (CDI):** recurrence of symptoms and a positive stool test for C. difficile infection [NAAT (PCR) or Enzyme immunoassay (EIA)] after a confirmed episode in the previous 8 weeks
- Severity classification of Clostridioides difficile infection (CDI):** The severity of CDI is based on laboratory studies and clinical features and is used to guide disposition, management, and prognosis.
- » Nonsevere CDI: leukocytosis $< 15,000$ cells/mm³ and serum creatinine < 1.5 mg/dL
 - » Severe CDI: leukocytosis $\geq 15,000$ cells/mm³ or serum creatinine ≥ 1.5 mg/dL
 - » Fulminant CDI: ≥ 1 criteria of severe CDI plus hypotension, shock, ileus, and/or toxic megacolon

Clinical features

- » Clinical symptoms typically develop during antibiotic treatment or 2–10 days following its initiation; however, 25–40% of cases manifest as late as 10 weeks following treatment.
- » **Diarrhea:** Most patients report mild to moderate greenish, foul-smelling watery diarrhea 3–15 times per day. The stools may have mucus but seldom gross blood. Rarely hematochezia and melena
- » **Lower abdominal cramping pain**, nausea, anorexia
- » **Abdominal tenderness**
- » Fever (uncommon) & dehydration (in severe cases)
- » **Fulminant disease occurs in up to 10% of patients.**
 - » Abdominal distention
 - » Severe hypovolemia due to toxic megacolon, paralytic ileus, lead to hypotension or shock

Diagnostic workup

- » **Clinical history, examination, and risk factors**
- » **CBC:** WBC increased.
- » **BUN, & creatinine:** may be elevated.
- » **Serum electrolytes:** Abnormal $\rightarrow$ hypokalemia
- » **Serum lactate** (Elevated), **Serum Albumin** (Low)
- » **Stool analysis & stool guaiac test** (Fecal occult test)
- » **Stool tests for toxins & toxigenic strains of C. difficile**
 - » Stool enzyme immunoassay (EIA) for C. difficile glutamate dehydrogenase antigen (GDH): **+ve**
 - » Stool NAAT (PCR) for C. difficile toxins: **+ve**
 - » EIA for C. difficile toxins A and B: **+ve**
- » Abdominal ultrasound and X-ray, CT abdomen
- » **Endoscopy (colonoscopy or flexible sigmoidoscopy):**
 - » Reveals pseudomembrane/colitis over colonic mucosa



TREATMENT OF C. DIFFICILE INFECTION

- » **For patients with initial disease (severe/non-severe)**
 - » Tab. Fidaxomicin 200mg (Dificid) x PO, BD for 10 days
 - » OR Cap. Vancomycin 125mg x PO, QID for 10 days.
 - » OR Tab. Metronidazole 500mg (Flagyl) x TDS x 10 days
- » **For patient with initial Fulminant disease**
 - » Cap. Vancomycin 125mg at dose 500mg x PO or via enteral tube x QID (every 6 hourly), for 48–72 hours, reduced to 125 mg PO, QID & continued for additional 10 days if there is clinical improvement.
 - » **Adjunct:** Tab. Metronidazole 500mg (Flagyl) x PO, TDS (Three times a day) for 10 days
 - » **Patient with paralytic ileus**, consider adding enemas of Inj. Vancomycin 500mg in 100mL 0.9%NS, PR x QID
- » **For patient with recurrent disease**
 - » **If the initial episode was treated with vancomycin:**
 - » Tab. Fidaxomicin 200mg (Dificid) x PO, BD, 10 days
 - » OR tapered & pulsed: Cap. Vancomycin 125mg PO QID for 10–14 days, then BD, for 1 week, then OD, for 1 week, and then every 2–3 days for 2–8 weeks
 - » **If the initial episode was treated with metronidazole:**
 - » Tab. Fidaxomicin 200mg (Dificid) x PO, BD, 10 days
 - » OR Cap. Vancomycin 125mg x PO, QID for 10 days.
- » **For patient with Subsequent recurrences**
 - » Tab. Fidaxomicin 200mg (Dificid) x PO, BD for 10 days
 - » OR Cap. Vancomycin 125mg x PO, QID for 10 days AND Tab. Rifaximin 200mg (Rifaxa) x 2Tablets, TDS x 20 days
 - » OR tapered & pulsed: Cap. Vancomycin 125mg as explain earlier in patient with recurrent disease

HICCUPS (SINGULTUS)

Name: _____ Age: _____ Sex: _____ Date: _____
 Temperature: _____ B.P: _____ Pulse: _____ Resp. Rate: _____

Definition: Hiccups refer to a sudden, involuntary contraction of the diaphragm that results in abrupt inhalations of air followed by a characteristic "hic" sound.

- » Singultus (hiccup) is common, usually transient, and only rarely indicative of disease.
- » If it persists, it can be highly bothersome, potentially interfering with sleep and leading to depression and physical exhaustion. It is presumed to be due to a disturbance in a reflex arc that includes the brainstem, the phrenic nerve, the vagus nerve, and the sympathetic chain.

CAUSES OF HICCUPS

Transient Hiccups (Second to minutes) » Stomach distension » Swallowed air » Smoking » Alcohol and carbonated beverages » Intense emotion (excitement/stress)	Chronic hiccups (> 1month) » Pericarditis » Laryngitis » Inflammation from the stomach from H.pylori » GERD » Space occupying lesions » Metabolic & CNS disorders » Medications » Idiopathic
Persistent Hiccups (>48 hours) » General anesthesia » Intubation	



Non-pharmacologic remedies used in the Emergency Department

- » Stimulation of the nasopharynx by applying forcible traction to the tongue, swallowing granulated sugar, gargling with water, sipping ice water, drinking from the far side of a glass, biting on a lemon, or inhaling noxious agents (e.g., ammonia)
- » C3-C5 dermatome stimulation by tapping or rubbing the back of the neck, coolant sprays
- » Direct pharyngeal stimulation by a nasal or oral catheter (90% effective)
- » Direct uvular stimulation by a spoon or cotton-tip applicator
- » Removal of gastric contents by means of emetics or a nasogastric tube

- » The following remedies lead to vagal stimulation (only one should be used at any given time):
 - » Iced gastric lavage
 - » **Valsalva maneuver:** an individual strongly exhales while holding their mouth and nose closed, generally effective for reducing the duration of transient hiccups, but they rarely resolve persistent or chronic hiccups.
 - » Carotid sinus massage (performed only by experienced personnel after exclusion of contraindications)
 - » Digital ocular globe pressure (performed only by experienced personnel after exclusion of contraindications)
 - » Digital rectal massage

Various techniques are used that interfere with normal respiratory function, such as the following:

- » Holding one's breath for several seconds
- » Hyperventilation
- » Gasping (as in fright)
- » **Breathing into a paper bag:**
Which increases arterial carbon dioxide tension (PaCO_2)
 1. Tightly press a small paper bag around your mouth
 2. Breathe slowly and deeply into it
 3. Repeat this several times, while keeping the paper bag in place.
- » **Drinks upside down:**
 1. Fill a glass with cold water
 2. Bend down at the waist and put your head down
 3. Slowly drink water from the opposite side of the glass, if required repeat it again.
- » Pulling the knees up to the chest and leaning forward
- » Using continuous positive airway pressure
- » Rebreathing 5% carbon dioxide
- » Mental distraction sometimes works. For example, the patient may be asked to "think of a loved one remembering you." An inventive naval doctor achieved success by offering \$10 if the patient could continue to hiccup immediately.

Pharmacological treatment for persistent hiccups

- » **Tab. Baclofen 10mg** (Lioresal, Baclast, Baclin, Liorex)
 - » Dose range: 5mg twice daily, to 10mg x four time daily
 - » Maximum daily dose: 60mg/day
- » **OR Cap. Gabapentin 300mg** (Neogab, Gabix) x TDS
 - » Dosage: 900mg to 1200mg in three divided doses
- » **OR Cap. Pregabalin 75mg** (Gabica, Zeegap) x BD
 - » Dosage: 75mg to 150mg/day in 2 divided doses
- » **OR Tab. Metoclopramide 10mg** (Maxolon, Metoclon) x PO x TDS
OR Inj. Metoclopramide 10mg (Maxolon, Metoclon) x IV x TDS
 - » Dosage: 10mg every 8 hourly up to 80mg/day
- » **OR Tab. Domperidone 10mg** (Motilium, Domel) x TDS
- » **OR Tab. Chlorpromazine 25mg** (Largactil) 25mg to 50mg per orally x TDS
- » **OR Inj. Chlorpromazine 25mg** (Largactil) 25mg to 50mg x IV, repeated 2-4 hours
- » **OR Tab. Haloperidol 1.5mg, 5mg** (Serenace, Dosik) x initially 1.5mg x TDS, then 5mg x BD
- » **OR Tab. Amitriptyline 25mg** (Tryptanol, Amyline, Amitin) x HS
 - » Dosage: 25mg to 100mg/day

IRRITABLE BOWEL SYNDROME (IBS)

Definition: IBS can be defined as an idiopathic clinical entity characterized by chronic (more than 3 months) abdominal pain that occurs in association with altered bowel habits. Approximately 2/3 of patients are women's.

△ IBS

C/C:

- Abdominal pain
 - » Frequency, intensity, and localization generally vary widely from patient to patient
 - » Typically related to defecation
- Altered bowel habits: Diarrhea and/or constipation
- Other GI tract symptoms: Nausea, reflux, early satiety, Passing of mucus, abdominal bloating
- Extraintestinal symptoms
 - » Generalized somatic symptoms: pain or fatigue, as in fibromyalgia
 - » Disturbed sexual function
 - » Dysmenorrhea
 - » Increased urinary frequency and urgency
- Psychosocial Abnormalities: More than 50% of patients with IBS who seek medical attention have underlying depression, anxiety, or somatization.
- Red flag symptoms: Nighttime diarrhea and abdominal pain, fever, bloody stools, weight loss and acute onset of symptoms!
- Physical examination: usually normal

Diagnostic criteria: Rome IV criteria for IBS

- All of the following criteria must be met to diagnose irritable bowel syndrome (IBS)
 - » Timing: ≥ 6 months since the onset of symptoms
 - » Symptoms
 - » Recurrent abdominal pain (≥ 1 day per week during the previous 3 months)
 - » PLUS ≥ 2 of the following
 1. Abdominal pain related to defecation
 2. Change in stool frequency
 3. Change in appearance of stool

Diagnostic workup

- Lab test: The following studies should routinely be considered to rule out alternative etiologies:
 - » All patients: CBC to screen iron deficient anemia
 - » In patients with diarrhea
 - Fecal calprotectin and Serum CRP
 - Serological test for Celiac disease (TG IgA)
 - Stool testing for giardiasis (Giardia antigen)
 - PCR tests: for multiple diarrheal organisms
 - » In patients with relevant symptoms and history
 - Thyroid function tests: Serum TSH
 - Test for infectious gastroenteritis: Stool D/R, stool culture, serum electrolytes, BUN/urea.
 - Stool microscopy to identify ova & parasites
- Colonoscopy: not recommended <45 w/o red flags
 - » Only recommended in patients: (>45 years)
 - With red flags for colorectal cancer (CRC)
 - Due for age-appropriate screening for CRC

Rx

General treatment

- Regular consultations and reassurance that the disease, although chronic, is benign
- Lifestyle changes: Regular Exercise, stress management, Dietary adjustments, Plenty of fluid, High-fiber foods and Psychological therapy
- Avoidance of Gas-bloating producing six foods: Fructose (corn syrups, apples, pears, honey, watermelon, raisins), lactose, fructans (garlic, onions, leeks, asparagus, artichokes), wheat-based products (breads, pasta, cereals, cakes), sorbitol (stone fruits), and raffinose (legumes, lentils, brussel sprouts, soybeans, cabbage).

(Peridots, Kalper, Mintec)

1. Cap. Peppermint oil formulations (Ref: CMD2-2024)
OR Tab. Mebeverine 135mg (Colofac, Spasler-P)
OR Tab. Mebeverine 200mg (Despas MR)
OR Tab. Chlordiazepoxide + Clidinium 2.5mg (Librax)
I - 0 - I (BD)
2. Cap. Omeprazole 40mg (Omega, Ruling, Risek)
OR Cap. Esomeprazole 40mg (Eskem, Esso, Nexum)
I - 0 - 0 (OD)
کھانے سے 30 منٹ پہلے
3. Cap. Fluoxetine 20mg (Flux, Depex, Depricap)
OR Tab. Escitalopram 10mg (Estar, Citanew)
OR Tab. Paroxetine CR 12.5mg or 25mg (Seroxat, Paraxyl CR)
I - 0 - 0 (OD)
ایک گولی صبح ناشتے کے بعد (One Cap. after breakfast)

For IBS-D:

- » Cap. Loperamide 2mg (Imodium) 2mg x 3-4 times/day
- » Tab. Rifaximin 550mg x (Rifixa, Nimixa) TDS for 2 weeks
- » Tab. Eluxadoline 75-100 mg twice daily (not available)

For IBS-C:

- » Fibrocol or Fibo powder sachets/Jar x BD
- » Polyethylene glycol sachets (Movcol, Movicol) x BD/TDS (17-34 g/day)

Classification of IBS

Several subtypes of IBS exist & are defined by stool quality

- IBS-D: Diarrhea is the predominant symptom
- IBS-C: Constipation is the predominant symptom
- IBS-M: Mixed diarrhea and constipation
- IBS-U: Criteria for IBS are met but bowel movements can't be categorized into the above subgroups

ULCERATIVE COLITIS

- Definition: Ulcerative colitis (UC) is a type of inflammatory bowel disease (IBD) characterized by chronic mucosal inflammation of the colonic mucosa of the rectum, colon, and cecum and a relapsing, remitting course.
- Etiology: The cause is unclear, but it seems to occur in genetically susceptible people in response to environmental triggers.
- Risk factors
 - » Genetic predisposition: E.g., HLA-B27 association
 - » Ethnicity: White populations, individuals of Ashkenazi Jewish descent
 - » Family history of inflammatory bowel disease (IBD)
 - » Episodes of previous intestinal infection
 - » Increased fat intake (especially saturated fat and animal fat)
 - » Use of oral contraceptives
 - » NSAIDs may exacerbate ulcerative colitis.
- Protective factors: Appendectomy, Smoking

CLASSIFICATION & ASSESSMENT

Montreal classification of ulcerative colitis

Montreal classification for the extent of ulcerative colitis based on endoscopic findings

Disease extent	Mucosal involvement
E1: Ulcerative proctitis	» Involvement limited to the rectum (proximal extent of inflammation is distal to the rectosigmoid junction)
E2: Left-sided ulcerative colitis	» Involvement limited to a portion of the colorectum distal to the splenic flexure
E3: Extensive ulcerative colitis	» Involvement extends proximal to the splenic flexure

Classification of ulcerative colitis by severity

There are several classification systems that can be used to assess disease severity.

Criteria include:

- » Endoscopic findings
 - Ulcerative colitis endoscopic index of severity (UCEIS)
 - Mayo endoscopic score
- » Clinical presentation
 - Simple clinical colitis activity index (SCCAI)
 - Truelove and Witts severity index for ulcerative colitis
- » A combination of both endoscopic findings and clinical presentation
 - Mayo score for ulcerative colitis activity
 - American College of Gastroenterology (ACG) ulcerative colitis activity index
- » Other: response to medication, disease course, and the patient's quality of life
- » Remission criteria (ACG): no diarrhea, no visible blood in stools, no fecal urgency, fecal calprotectin < 150–200 mcg/g, normal laboratory values, and normal endoscopy findings

Ulcerative colitis – Assessment & index of disease activity by American college of gastroenterology

Criteria	Severity of ulcerative colitis		
	Mild	Moderate-to-severe	Fulminant
» Stools per day	< 4	> 4	> 10
» Frequency of blood in stool	Intermittent	Frequent	Continuous
» Hemoglobin	Mild, occasional	Often	Continuous
» ESR	Normal	< 75% of normal	Transfusion required
» CRP	< 30 mm/hour	> 30 mm/hour	
» Fecal calprotectin		Elevated	
» Mayo endoscopy score		> 150–200 mcg/g	
» Ulcerative colitis endoscopic index of severity	1	2–4	3
		1–2	7–8
		5–8	

Truelove and Witts severity index

Criteria	Mild	Severe
	≤ 4	≥ 6
» Bowel movements per day	Small amount	Macroscopic blood
» Amount of blood in stool	No fever	≥ 100.4°F (37.8°C)
» Temperature	No tachycardia	> 90 bpm
» Heart rate	No severe anemia	≤ 75% of normal
» Hemoglobin	≤ 30 mm/hour	> 30 mm/hour
» ESR		

Clinical features

- Intestinal symptoms: Rectal bleeding, Diarrhea with mucus, Fecal urgency, Abdominal pain/cramps, Tenesmus
- Extraintestinal symptoms
 - Skeletal (most common): osteoarthritis, ankylosing spondylitis, sacroiliitis
 - Ocular: Uveitis, episcleritis, iritis
 - Biliary: primary sclerosing cholangitis (PSC) - Rare for patients with UC to develop PSC, but up to 90% of all patients affected by PSC will also be affected by UC.
 - Cutaneous: Erythema nodosum, pyoderma gangrenosum, aphthous stomatitis
 - General: Fatigue, fever, weight loss

Diagnostic workup

- Blood investigation
 - CBC: variable degree of anemia, leukocytosis or thrombocytosis
 - Inflammatory markers: ESR, CRP: ↑ levels may indicate active UC and often correlates with disease severity.
 - Hypoalbuminemia: associated with a poor prognosis and more severe disease
 - LFTs: ↑ ALP, Bilirubin AST, ALT in patients with concurrent primary sclerosing cholangitis (PSC).
 - Basic metabolic panel (BMP): Hypokalemic metabolic acidosis; elevated sodium and BUN.
 - Perinuclear ANCA (pANCA): Routinely NOT recommended. Elevated in up to 70% of patients with UC.
- Stool investigation
 - Stool test for clostridium difficile infection (CDI)
 - PCR panel for other enteric infections: depending on the patient's symptoms and risk factors for diarrhea
 - Stool culture and microscopy: to assess for bacteria and ova and parasites if a stool PCR panel is not available
 - Fecal calprotectin: can help assess for mucosal inflammation
- Endoscopy: ileocolonoscopy with biopsy
- Abdominal x-rays: Usually normal in mild-to-moderate disease. Loss of colonic haustra (lead pipe appearance) may be seen in severe cases.
 - May show signs of complications, e.g.:
 - Toxic megacolon: Massive distention
 - Ulceration: Segmental dilation with irregular edges outlined by gas
 - Perforation: Pneumoperitoneum
- Abdominal ultrasound
- Order when complications or other diagnoses are being considered: CT scan or MRI abdomen



TREATMENT OF ACUTE SEVERE ULCERATIVE COLITIS (ASUC)

- Hospitalized the patient.
- Obtain all routine investigation include CBC, LFTs, serum albumin, ESR, CRP, stool test for clostridium difficile infection (CDI), abdominal X-ray, abdominal Ultrasound and CT or MRI abdomen as indicated.
- Monitor vital signs and closely monitor complication using serial abdominal examinations and abdominal x-rays
- Consult gastroenterology to obtain urgent flexible sigmoidoscopy (ideally within 24 hours) and discuss treatment
- Start IV corticosteroids: Inj. Methylprednisolone (Solu-Medrol) at dose 1mg/kg (maximum dose 60-80mg/day) x IV x OD for up to 7 days. Patients who do not achieve remission after 3-5 days of IV corticosteroids, consider cyclosporine 2 mg/kg x IV, OD or infliximab 5 mg/kg x IV given at weeks 0, 2, and 6 initially, followed by 5 mg/kg every 8 weeks
- DVT prophylaxis: Inj. Enoxaparin sodium 60mg or 80mg (Clexane) x 100 IU/kg (1.5mg/kg) x SC x OD
- Other supportive measures, if indicated such as blood transfusion, fluids, and electrolyte replacement.



TREATMENT OF MILD TO MODERATE ULCERATIVE COLITIS (UC)

- Firstline: 5-aminosalicylic acid (5-ASA): Topical Mesalamine is the drug of choice and is superior to topical corticosteroids and oral 5-ASA [Tab. Mesalamine 800mg (Masacol), Tab. Sulfasalazine 500mg (Salazopyrin)]
- Proctitis: rectal mesalamine suppository 1g per rectal (PR) x once daily (OD), at bedtime OR mesalamine enema x 4g (5 tablets of Masacol) per rectal (PR), OD at bedtime, for proctosigmoiditis, for 4-8 weeks.
- Left-sided or extensive colitis: Tab. Mesalamine 800mg (Masacol) at dose 2.4g (3 tablets), orally, once daily (OD) PLUS, rectal mesalamine enema at dose 4g (5 tablets of Masacol) per rectal (PR), OD at bedtime.
- Corticosteroids can be used for patients who can't tolerate 5-ASA therapy or don't get better with it alone.

- » Patient with proctitis: Rectal budesonide at dose 2mg PR, BD for 2 weeks, then 2mg PR, OD at bedtime OR Hydrocortisone enema or foam at dose 80–100 mg PR, OD at bedtime.
- » OR Oral Tab. Budesonide MMX (Cortiment®MMX®) at dose 9mg per orally (PO), once daily (OD)
- » OR Oral Tab. Prednisolone 5mg (Deltacortril, Rapicort) at dose 40–60 mg per orally (PO), once or twice daily
- » Supportive treatment:
 - » With abdominal pain/cramps: Tab Mebeverine 135mg (Colofac, Spasler-P) x per orally (PO) x TDS
 - » With fever/analgesia: Paracetamol 500mg (Panadol) at dose 500–1000mg x TDS/SOS
 - » Consider anxiolytics, and sedatives: Tab. Alprazolam 0.5mg (Xanax, Alp) at bedtime. (max dose 3mg/day)
 - » Multivitamins/Micronutrients support: Identify and treat any vitamins deficiency.
 - » Probiotics has no role, currently, *poor insufficient evidence supports using probiotics therapy.*

Rx

TREATMENT OF MODERATE TO SEVERE ULCERATIVE COLITIS (UC)

- » Tab. Budesonide MMX (Cortiment®MMX®) at dose 9mg per orally (PO), once daily (OD)
- » OR Tab. Prednisolone 5mg (Deltacortril, Rapicort) at dose 40–60 mg per orally (PO), once or twice daily
- » OR Anti-Tumor necrosis factor (TNF) therapy: Infliximab, adalimumab, golimumab with or without azathioprine
- » OR Integrin receptor antagonist: Vedolizumab
- » OR Janus kinase inhibitors (JAK3 inhibitor): Tofacitinib, Upadacitinib
- » OR Sphingosine 1-phosphate receptor modulator: Ozanimod
- ❖ Note: The preferred agent depends on several considerations: prior exposure and response to biologic agents; disease severity; patient comorbidities; preferred mode of administration (intravenous, subcutaneous, oral); and pharmacy/insurance company tiering.

SURGICAL TREATMENT

- » Curative approach with full recovery
- » Reduce risk of colorectal cancer
 - » Indications
 - » Emergent surgery: Acute complications despite adequate conservative management, consult surgery if complication arise such as toxic megacolon, perforation, sepsis, uncontrolled bleeding, multiorgan failure OR There is no improvement after 3–5 days of medical management
 - » Elective surgery: epithelial dysplasia, severe relapses, long-term dependence on steroids, impairment of the patient's general condition
 - » Procedure: proctocolectomy with an ileal pouch-anal anastomosis (IPAA or 'J' pouch)

LONG-TERM MANAGEMENT OF ULCERATIVE COLITIS

1. Disease Monitoring
 - » Assess Treatment Response: Use endoscopy or fecal calprotectin if endoscopy is not possible.
 - » Flexible Sigmoidoscopy: Recommended 3–6 months after starting a new treatment.
 - » Follow-Up: Every 3 months until remission is achieved, then every 6–12 months.
2. Colorectal Cancer Screening
 - » Start Screening: 8–10 years after the initial diagnosis, or at the time of diagnosis of PSC.
 - » Modality: ileocolonoscopy with biopsies.
 - » Interval: Every 1–5 years.

Treatment Guideline (CMDT-2024)

Treatment Guideline: Systemic effects from short-term use are very slight. For patients with distal disease who do not improve with topical or oral mesalamine therapy within 6 weeks, the following options may be considered: (1) a combination of a topical agent with an oral 5-ASA; (2) rectal corticosteroid; or (3) addition of oral Prednisolone or budesonide MMX 9 mg/day for 4–8 weeks to rectal and oral 5-ASA. Most patients with proctitis or proctosigmoiditis who achieve complete remission with oral or rectal 5-ASA should continue indefinitely on the same therapy to reduce the likelihood of symptomatic relapse. Maintenance treatment with 5-ASA reduces the 12-month relapse rate from 75% to less than 40%. Some patients, however, may prefer intermittent therapy for symptomatic relapse. Topical corticosteroids are ineffective for maintaining remission of distal colitis. NSAIDs, opioids, and anticholinergics should be avoided in ASUC. Azathioprine may be considered in combination with anti-TNF therapy for induction of remission or as monotherapy for maintenance of remission; it is not recommended as monotherapy for induction of remission. Systemic corticosteroids should only be used for induction of remission. Steroid-sparing agents are preferred for maintenance of remission.

CROHN DISEASE (CD)

- Introduction: Crohn disease (CD) is an inflammatory bowel disease (IBD) of unclear etiology. 1/3 of cases of Crohn disease involve the small bowel only, most commonly the terminal ileum (ileitis). Half of all cases involve the small bowel and colon, most often the terminal ileum and adjacent proximal ascending colon (ileocolitis).
- Cause: Immune dysregulation and dysbiosis, which promotes chronic inflammation, the ultimate cause of which is not fully understood. Risk factors: Familial aggregation, Genetic predisposition (e.g., mutation of the NOD2 gene, HLA-B27 association) and tobacco smoke

CLINICAL FEATURES

- Crohn disease (CD) typically has a chronic intermittent course with episodic acute flares & periods of remission.
- Clinical features differ according to the severity of CD.
- Patients with mild CD may be asymptomatic while patients with fulminant CD have severe symptoms.
- Constitutional Symptoms:** Low-grade fever, weight loss and Fatigue
- Gastrointestinal Symptoms:** CD most commonly affects the terminal ileum and colon, but involvement of any part of the GI tract (from mouth to anus) is possible. In contrast to ulcerative colitis, rectal involvement is uncommon.
- Chronic diarrhea
- Lower gastrointestinal bleeding (uncommon)
- Abdominal pain, typically in the RLQ
- Palpable abdominal mass in the RLQ
- Features of CD complications**
 - Malabsorption: Weight loss, anemia, failure to thrive
 - Enterocutaneous or perianal fistulas, often associated with abscess formation
- Extraintestinal symptoms:** Extra-intestinal manifestations of CD are present in 20–30% of patients with CD.
 - Joints:** Enteropathic arthritis
 - Nail clubbing**
 - Eyes:** Uveitis, Iritis, Episcleritis
 - Liver/bile ducts:** Cholelithiasis
 - Urogenital system:** Urolithiasis (Mostly calcium oxalate stones)
 - Oral mucosa:** Oral aphthae & Pyostomatitis vegetans
 - Skin:** Erythema nodosum, Acrodermatitis enteropathica and Pyoderma gangrenosum

DIAGNOSTICS WORKUP

1. Radiological tests

- Initial Test:** Ultrasound abdomen → Supportive finding (of active disease): bowel wall thickening (> 4 mm)
- Colonoscopy** usually is performed first to evaluate the colon & terminal ileum & to obtain mucosal biopsies.
- CT Enterography OR MR Enterography** is obtained in patients with suspected small bowel involvement.
- CT abdomen & pelvis (with IV contrast):** preferred in acutely ill patients who cannot tolerate PO contrast
- Small bowel follow-through:** can identify luminal complications such as internal fistulas and narrowed segment(s) of bowel (string sign)
- Plain X-ray abdomen:** Consider for expedited assessment of complications.
- CT Enteroclysis or MRI Enteroclysis:** Consider for evaluation of an acute flare or response to therapy.
- MRI abdomen and pelvis (with IV contrast):** Preferred modality to evaluate for perianal fistulas, Consider for stable patients with suspected intraabdominal abscesses

2. Laboratory tests

- To rule out differential diagnoses of crohn disease (CD)
 - Stool D/R:** to identify ova, cysts, or clostridium difficile infection in symptomatic patients
 - Serology:** not routinely recommended due to low sensitivity.
 - ↑ Anti-Saccharomyces cerevisiae antibodies (ASCA):** more commonly elevated in CD than in UC
 - pANCA:** More commonly elevated in ulcerative colitis (UC) than in crohn disease (CD)
- To monitor disease activity
 - Fecal calprotectin and/or fecal lactoferrin:** proteins associated with neutrophil activation
 - Used as noninvasive markers of intestinal inflammation to monitor disease activity and response to therapy. Also used to differentiate IBD from irritable bowel syndrome (IBS)
 - Inflammatory markers:** serum CRP, serum ESR & platelets count
 - CRP correlates with disease activity better than ESR; both may be normal in patients with mild CD.
 - Thrombocytes may be an indicator of active disease (reactive thrombocytosis)
- To identify complications
 - To evaluate for anemia & micronutrient deficiency: CBC (↓ Hb, ↓ MCV), Iron studies, vitamin B12

- ✎ To identify malnutrition: ↓ Total protein, ↓ Albumin & Calcium maybe ↓
- ✎ End-organ damage: ↑ Serum creatinine and ↑ Serum Urea
- ✎ Dehydration: Serum electrolytes (derranged serum electrolytes)
- ✎ Stool studies: Stool culture, Clostridium difficile toxin, Ova & Parasite study, fecal calprotectin



Treatment of Crohn's Disease

1. Induction of Remission: (علامات کو کم کرنا اور مرض کو قابو میں لانا)

Mild to Moderate Crohn's Disease:

- » Limited to the ileum and right colon: controlled ileal release Budesonide at dose 9 mg orally once daily for up to 6 weeks, followed by tapering. If there is no response to budesonide within 2 weeks, the patient should be switched to **prednisolone** (as dosage below)
- » Colonic disease: Oral Corticosteroids – Tab. **Prednisolone 5mg** (Deltacotril) at dose 40-60mg per orally daily for 1-2 weeks, reducing by 5 mg per week to 20 mg, then by 2.5-5mg/week until discontinuation.
- » Antibiotics: Start Empiric antibiotic therapy if an abscess or fistulizing disease or perianal disease
 - ✎ Tab. Metronidazole 400mg (Flagyl) x per orally three times daily (TDS).
 - ✎ PLUS, Tab. Ciprofloxacin 500mg (Cipesta, Novidate) x per orally twice daily (BD)

Moderate to Severe Crohn's Disease:

- » 1. Oral Corticosteroids: Tab. **Prednisolone 5mg** (Deltacotril) at dose 40-60mg per orally daily for 1-2 weeks, reducing by 5 mg per week to 20 mg, then by 2.5-5 mg per week until discontinuation.
- » 2. PLUS, an immunomodulator: Tab. **Azathioprine 50mg** (Imuran) at dose 2-2.5 mg/kg/day per orally.
- » OR Monotherapy with Biologics agent:
 - ✎ Inj. Infliximab: 5 mg/kg IV infusion at 0, 2, and 6 weeks, followed by every 8 weeks.
 - ✎ Inj. Adalimumab: 160 mg x SC on day 1, then 80 mg at week 2, followed by 40 mg every two weeks.
 - ✎ Inj. Certolizumab pegol: 400 mg x SC at weeks 0, 2, and 4, followed by every 4 weeks.
 - ✎ Inj. Ustekinumab: 6 mg/kg IV infusion at week 0, followed by 90 mg subcutaneously every 8 weeks.
 - ✎ Inj. Vedolizumab: 300 mg IV infusion at weeks 0, 2, and 6, followed by every 8 weeks.
 - ✎ Inj. Methotrexate: 25 mg x SC once weekly for steroid-dependent patients, subcutaneous (SC) administration has better bioavailability than per orally.

Severe to fulminant Crohn's Disease: Hospitalization, Early surgery consultation, Nutritional support, IV fluid therapy, IV Inj. methylprednisolone (solu-medrol) at dose 40-60 mg IV once daily PLUS, Infliximab

2. Maintenance of Remission: (مرض کو قابو میں رکھنے کا مرحلہ)

جب علامات قابو میں آجاتی ہیں تو طویل مدتی علاج دیا جاتا ہے تاکہ بیماری دوبارہ نہ ہو۔

Immunomodulators:

- » Tab. Azathioprine 50mg (Imuran) at dose 2-2.5 mg/kg/day per orally.
- » OR Tab. 6-Mercaptopurine (6-MP) at dose 1-1.5 mg/kg/day per orally.
- » OR Inj. Methotrexate at dose 15-25 mg x SC once weekly for maintenance of remission.

Biologics: Combination therapy of anti-TNF PLUS an immunomodulator is preferred over monotherapy

- » anti-TNF-α antibodies: Inj. Infliximab: at dose 5 mg/kg IV infusion every 8 weeks. OR Inj. Adalimumab: at dose 40 mg subcutaneously (SC) every 2 weeks. OR Inj. Certolizumab pegol: at dose 400 mg subcutaneously (SC) every 4 weeks.
- » Anti-leukocyte trafficking antibody: Inj. Vedolizumab at dose 300 mg IV infusion every 8 weeks.
- » Anti-p40 antibody: Inj. Ustekinumab at dose 90 mg subcutaneously every 8 weeks.

Corticosteroids: Not recommended for long-term maintenance due to risk of significant side effects.

3. Adjunctive therapy and supportive care:

- » Smoking Cessation: should be strongly counselled to stop smoking to improve outcomes.
- » Identify and treat deficiencies: vitamins b12, folic acid, zinc, calcium, iron and vitamin-D)
- » Oral Calcium and vitamin-D supplements: should be co-prescribed in patients who are on corticosteroids.
- » Parenteral vitamin B12 (mecobalamin) at dose 1000mcg x SC or IM per month
- » Nutritional Therapy: Enteral nutrition with either an elemental (constituent amino acids) or polymeric (liquid protein) diet may induce remission. Both types of diet are equally effective.
- » For pain: use atypical opioids (e.g., tramadol) if opioids are necessary. NSAIDs avoidance.
- » Stress, depression, and anxiety management: SSRIs (Escitalopram, Paroxetine) – psychiatry section
- » Antidiarrheal therapy: Cap. Loperamide 2mg (Imodium) at dose 4 mg followed by 2 mg after each unformed stool until diarrhea is controlled, OR Cholestyramine 1-2 g PO daily. Antidiarrheals should not be used in patients with bowel obstruction, abdominal tenderness, or signs of systemic infection (e.g., fever)
- » Prior to anti-TNF therapy, latent tuberculosis must be excluded as well as hepatitis B, hepatitis C, HIV and VZV status, as well as immunization status, as

CELIAC DISEASE

Name: _____ Age: _____ Sex: _____ Date: _____
Temperature: _____ B.P: _____ Pulse: _____ Resp. Rate: _____

- Definition: Celiac disease is a permanent dietary autoimmune disorder characterized by an intestinal hypersensitivity to gluten, a grain protein that results in diffuse damage to the proximal small intestinal mucosa with malabsorption of nutrients.
- Synonyms: also called sprue, celiac sprue, and gluten sensitive enteropathy

ETIOLOGY

- Genetic predisposition with association to HLA antigens
 - HLA-DQ2 in 90–95% of patients
 - HLA-DQ8 in 5–10% of patients
- Consuming gliadin from grains such as wheat, rye, and barley leads to an autoimmune reaction within the small intestinal wall.
- Commonly associated with autoimmune diseases

CLINICAL FEATURES

- Gastrointestinal symptoms
 - Chronic or recurring diarrhea
 - Flatulence, abdominal bloating, and abdominal pain/discomfort
 - Nausea/vomiting
 - Lack of appetite
 - Constipation (rarely)
- Extraintestinal symptoms and associations
 - Classic symptoms of malabsorption:** Diarrhea, steatorrhea, abdominal distention, weakness, weight loss, fatigue, vitamin deficiency, iron deficiency anemia, osteoporosis/osteopenia, hypocalcemia
 - More commonly present in infants (younger than 2 years).
 - Older children and adults are less likely to manifest signs of serious malabsorption.
 - In children:** Failure to thrive, growth failure, delayed puberty
 - Dermatologic associations:** Dermatitis herpetiformis
 - Neuropsychiatric symptoms:** Peripheral neuropathies (numbness, burning and tingling of the hands and feet), headache, ataxia, depression, irritability.
 - Gynecological associations:** reduced fertility or infertility
 - Endocrine associations:** Autoimmune thyroid disease, type 1 diabetes mellitus
 - Associated chromosomal syndromes:** Turner syndrome, Down syndrome
 - Other associated conditions:** autoimmune hepatitis, irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), rheumatoid arthritis, sarcoidosis, selective IgA deficiency, autoimmune thyroid disease

DIAGNOSTIC WORKUP

General principles of the diagnosis of celiac disease

- Celiac disease is an underdiagnosed condition that requires a high index of suspicion.
- Diagnosis is based on serology (initial testing) and EGD with duodenal biopsy (confirmation).
 - A gluten-free diet can cause negative test results.
 - HLA-based testing and/or a gluten challenge are options for patient's not consuming gluten.
- Common indications for testing include:
 - Symptoms of malabsorption such as steatorrhea
 - First-degree relatives with celiac disease
 - Iron deficiency anemia unresponsive to treatment
 - Elevated liver enzymes with no discernable cause
 - Type-1 diabetes mellitus
 - Signs of osteoporosis such as repeated or unexplained fractures
- Workup of other autoimmune disorders: autoimmune-thyroiditis, autoimmune-hepatitis



DIAGNOSTIC WORKUP

- **IgA tissue transglutaminase antibody (tTG IgA):** Initial test, crucial part of celiac disease serology
 - » Widely available test with high specificity ($\geq 96\%$)
 - » Risk of false negatives (e.g., in IgA deficiency, gluten-free diet)
- **Total IgA (or Quantitative IgA):** Indicated for all patients because of the high prevalence of IgA deficiency in patients with celiac disease (approximately 2–3%). If patients have low IgA, perform further IgG-based testing.
- **IgG Deamidated gliadin peptide (IgG DGP):** Indicated in IgA deficiency or discordant biopsy and serology
- **Complete blood count (CBC):** Low Hb and microcytic hypochromic RBCs
- **Anti-endomysial antibody (EMA):** Potential second-line confirmatory test (high-specificity but lower sensitivity)
- **HLA testing:** 2nd line testing after unclear initial evaluation. Assesses for haplotypes HLA-DQ2 and HLA-DQ8
- **Skin biopsy:** Order this test initially in any patient with skin lesions suggestive of dermatitis herpetiformis. May show granular deposits of IgA at the dermal papillae of lesional & perilesional skin by direct immunofluorescence
- **EGD (EsophagoGastroDuodenoscopy) with small intestine biopsy (confirmatory test)**
 - » **Indications:** positive serology or high clinical suspicion despite negative serology
 - » At least five duodenal biopsies should be taken (with ≥ 1 from the duodenal bulb).
 - » **Histological findings:** typically ranked by severity according to the Marsh classification.
 - ↳ Intraepithelial lymphocytic infiltration
 - ↳ Crypt hyperplasia
 - ↳ Villous atrophy
- **Further investigation**
 - » **Gluten challenge:** may be indicated if patients are already adhering to a gluten-free diet
 - Systematic reintroduction of gluten into a patient's diet prior to (repeated) serologic & endoscopic testing
 - 3 g gluten per day for up to eight weeks OR until the patient develops characteristic symptoms
 - » **Nutrient/vitamins deficiency screening (individualize)** → indicated in confirmed celiac disease such as iron profile (serum ferritin), zinc, calcium level, serum vitamin b12, b6, folate level, serum vitamin-d level
 - » **Associated autoimmune disorders:** Consider further testing if there are symptoms for thyroiditis, autoimmune hepatitis, and/or diabetes mellitus.
 - » **Tests for malabsorption:** Not routinely indicated (low sensitivity and specificity)
 - **D-xylose absorption test:** Low urine d-xylose levels (The passive absorption of d-xylose in the proximal small intestine is impaired by the mucosal defect and bacterial overgrowth.)
 - **Fat malabsorption:** Quantitative stool fat assays or qualitatively via fat stains (e.g., Sudan III stain)
- **Follow-up**
 - » Repeat laboratory studies after 3–6 months and 12 months, then annually
 - tTG-IgA or DGP antibodies
 - Nutrient levels if the patient had a deficiency at the time of diagnosis
 - » **Endoscopy:** only if symptoms persist or return in patients adhering to a gluten-free diet



TREATMENT OF CELIAC DISEASE

Diet

- » **The only accepted treatment of celiac disease is a strict lifelong gluten-free diet.**
 - ↳ Abstain from products containing wheat, rye, barley, or spelt.
 - ↳ Symptoms usually improve quickly
- » **Dietary advice and counseling:**
 - ↳ The diet should not be started until definitive diagnosis has been made by small intestinal histology.
 - ↳ After diagnosis, the patient should be referred to a dietitian with specific training in celiac disease and the gluten-free diet. Celiac disease patients are at risk of becoming overweight/obese.
 - ↳ **Recommended foods:** rice, corn, potatoes, soybeans, millet
 - ↳ **Patients with secondary lactase deficiency:** Avoid milk products.
- **Supplementation:** Iron and vitamin supplementation, if there are deficiencies such as iron deficiency anemia, vitamin d deficiency, vitamin b12 deficiency and folate deficiency.
- **Consider Bone mineral density** should be evaluated after approximately 1 year on a gluten-free diet to assess for osteopenia or osteoporosis screening in adult patients
- **Failure to respond to therapy/refractory celiac disease:** Referral to a gastroenterologist

MALABSORPTION

Name: _____ Age: _____ Sex: _____ Date: _____
 Temperature: _____ B.P: _____ Pulse: _____ Resp. Rate: _____

Introduction:

- Despite the distinct underlying pathological mechanisms of malabsorption and maldigestion, the term malabsorption is used to refer to both disorders in clinical practice. **Malabsorption** (e.g., celiac disease, lactose intolerance) describes a malfunction of the intestinal wall, resulting in the insufficient absorption of breakdown products. **Maldigestion** (e.g., exocrine pancreas insufficiency or cholestasis) is caused by an intraluminal disorder (insufficient secretion of pancreatic enzymes or bile), which prevents the adequate breakdown of food in the intestinal lumen. Both disorders can lead to malnourishment, which, in children, may manifest with delayed and inadequate physical development. Adults mainly present with chronic diarrhea, weight loss, and signs of malnutrition (e.g., iron deficiency anemia).

Definition: Malabsorption disorders can be caused by either the insufficient absorption or digestion of nutrients. The condition can be further defined as global or partial.

- Global malabsorption** in diseases causing diffuse mucosal damage or a reduction of the absorptive surface (celiac disease)
- Partial malabsorption** caused by a localized absorption impairment, resulting in deficiencies of specific nutrients (e.g., vitamin B12 deficiency in patients with diseases affecting the terminal ileum)

Clinical features

1. General symptoms

- Global malabsorption**
 - Diarrhea (most common), steatorrhea, abdominal distention, flatulence, weight loss, fatigue
 - Additional symptoms of specific deficiencies
- Partial (isolated) malabsorption:** only symptoms specific to individual nutrient deficiencies (e.g., impaired cobalamin absorption with megaloblastic anemia)

2. Features due to deficiencies

- Deficiency of fat-soluble vitamins:** Vitamin 'A' deficiency and Vitamin 'D' deficiency (Osteomalacia and rickets)
- Deficiency of water-soluble vitamins:** vitamin-B1, B2, B3, B5, B6, B7, B12 & vitamin-C.
- Zinc deficiency:** immune dysfunction, impaired wound healing, hypogonadism, diarrhea, perioral dermatitis, alopecia, abnormal taste, and smell
- Protein:** edema, cachexia
- Iron deficiency anemia or microcytic anemia**
- Electrolytes:** hypokalemia or hypocalcemia

Diagnostic workup

- CBC:** macrocytic anemia (decrease vitamin B12 or folate) and/or microcytic anemia (decrease iron)
- Serum Cholecalciferol/vitamin-D3 level:** ↓
- Serum zinc level:** ↓
- Serum total protein and albumin:** ↓ (edema)
- Serum calcium or magnesium:** ↓
- Serum carotene or vitamin-A:** ↓
- Stool analysis:** Analysis of fecal fat; over 72 hours (e.g., using Sudan stain) → Detection of pathogens
- D-xylose absorption test:** Assesses the absorptive function of the upper small intestine
 - Method:** The patient fasts overnight, then 25g of D-xylose is administered orally.
 - Then:**
 - Urine is collected over 5 hours. Considered abnormal if urine D-xylose levels < 4g/5 hour.
 - Blood sample is collected after 1 hour. Considered abnormal if serum D-xylose levels < 20 mg/dL.
- Hydrogen breath test:** Assess the intestinal absorption of individual carbohydrates
 - Lactulose breath test:** Determination of orocecal transit time (small intestine transit time)
 - Glucose hydrogen breath test:** If abnormal bacterial colonization of the small intestine is suspected
- Further testing (for underlying diseases):** E.g., celiac disease or lactose intolerance, vitamin deficiencies

Rx

- Identification and treatment of underlying cause

Symptomatic treatment

- Oral supplementation of fluid, nutrients, and deficient vitamins
- Advice caloric and protein-enriched diet
- IV nutrition therapy in severe cases (e.g., following extensive intestinal resection)



SMALL INTESTINAL BACTERIAL OVERGROWTH (SIBO)

Name:

Temperature:

Age:

B.P.:

Sex:

Pulse:

Date:

Resp. Rate:

- Definition:** a pathologically increased growth of bacteria in the small intestine
- » The small intestine normally contains a small number of bacteria.
 - » Bacterial overgrowth in the small intestine of whatever cause may result in malabsorption via several mechanisms.
 - » Passage of malabsorbed bile acids and carbohydrates into the colon leads to an osmotic and secretory diarrhea and increased flatulence.

Etiology

(ACG Clinical Guideline 2020-21, CMDT-2023)

Anatomic causes/abnormalities	Motility disorders	Medications
» Short bowel syndrome » Afferent limb syndrome (Billroth-II gastrectomy) » Resection of ileocecal valve » Blind loop syndrome: bacterial overgrowth in the bypassed intestinal segment (blind loop) that occurs as a result of gastrectomy » Small intestine diverticulosis » Inflammatory bowel disease	» Vagotomy » Diabetic enteropathy » Scleroderma (systemic sclerosis) » Irritable bowel syndrome » Chronic intestinal pseudo-obstruction	» Chronic use of proton pump inhibitor (PPI) therapy → gastric achlorhydria → a condition in which the stomach does not produce hydrochloric acid.

Pathophysiology: all resulting from bacterial overgrowth

- » Decreases absorption of vitamin B12, fat-soluble vitamins (A,D,E,K), zinc, and iron
- » Increases production of folate
- » Increases deconjugation of the bile acid

Clinical features	Diagnostic workup
» Diarrhea » Bloating and flatulence » Abdominal discomfort » Sometime steatorrhea (bulky, light-colored stools) with weight loss » Malabsorption (see above) » Bacterial overgrowth should be considered in any patient with these symptoms, especially patients with a predisposing cause (such as prior GI surgery) and older adults with unexplained diarrhea and weight loss. » Bacterial synthesis of folic acid and consumption of cobalamin may cause elevated serum folate and decreased vitamin B12 levels. » Severe cases may result in clinically significant vitamin and mineral deficiencies, including fat-soluble vitamins A or D, and low serum albumin	» CBC: anemia » Jejunum aspirate cultures collected during endoscopy → (A specific diagnosis can be established firmly only by an aspirate and culture of distal duodenal secretion that demonstrates over 10^3 organisms/mL). » Positive lactulose breath test » Hydrogen breath test and methane tests with glucose or lactulose as substrates are generally preferred because of their ease of use → Following ingestion of glucose 75g or lactulose 10g, a rise in exhaled breath hydrogen of 20 ppm or methane of 10 ppm or more within 90 minutes is suggestive of bacterial overgrowth and has 65% diagnostic agreement with small bowel cultures. » Small bowel study → CT or MR enterography, barium radiography may be obtained to look for mechanical factors predisposing to intestinal stasis.



TREATMENT OF SMALL INTESTINAL BACTERIAL OVERGROWTH (SIBO)

- » Where possible, the anatomic defect that has potentiated bacterial overgrowth should be corrected.
- » **Oral broad-spectrum antibiotics for 7-10 days** improves symptoms in up to 90% of patients for weeks to months.
- » Parenteral supplementation of vitamins and proteins
- » **Recommended regimens include ONE of the following:**
 - » Tab. Rifaximin 550mg (Rifaxa, Nimixa) x Three times daily
 - OR Tab. Ciprofloxacin 500mg (Cipesta, Novidate) x Twice daily (BD)
 - OR Tab. Co-Trimoxazole (Septran DS, Bactrim forte) x Twice daily (BD)
 - OR Tab. Metronidazole 400mg (Klint, Flagyl) x Twice daily (BD)
 - OR Tab. Co-amoxiclav 1g (Augmentin, Amclav) x Twice daily (BD)

ADULTS CONSTIPATION

Name:

Age:

Sex:

Date:

Temperature:

B.P:

Pulse:

Resp. Rate:



- C/C:**
- » Abdominal pain/spasm
 - » Inability to defecate for days or weeks
 - » Normal bowel sounds
 - » Distended, tympanic abdomen

Digital Rectal Examination: hard, impacted stools distending the rectum

US whole abdomen & Pelvis

Abdominal x-rays erect & supine (to rule out bowel perforation)

Findings:

- » Dilated bowel loops
- » Fecal shadows in the colon and rectum
- » Air-fluid levels may be visible.

Investigation:

- » CBC
- » Urea, creatinine & electrolytes

Dosage/Warnings of Enema

- » Using more than one enema in 24 hours can be harmful.
- » **Not for more than 3 days**
- » **Use in caution:** kidney disease and heart diseases, > 55 years

Contraindication of enema

1. Rectal bleeding/piles/fissure
2. Gastric/intestinal bleeding
3. Acute inflammation and ulcerous in the colon or anus
4. Pregnancy
5. Rectal cancer
6. Intestinal perforation

Indication of enema

- » Treat constipation.
- » Treat impacted bowels.
- » Clean the bowel.
- » Prep for surgery.
- » Prep for x-rays.
- » Prep for endoscopy.



OUTPATIENT/OPD TREATMENT OF ADULT'S CONSTIPATION

- » Identify and treat any underlying conditions
- » **Lifestyle changes:**
 - » High-fiber diet
 - » **Increased water intake:** 8-10 glass per day
 - » Regular Exercise on daily basis

1. **Syp. Lactulose** (Lilac, Duphalac)
15ml to 60ml 4-6hourly then 30ml x PO x OD
OR sodium Picosulphate (Tab/Syp. Laxoberon, Tab/drops Conspic)
If Diabetic Tab Laxoberon OR Drops/Tab. Skilex

2. **Tab. Drotaverine 80mg** (Nospa forte, Relispa forte)
1 - 0 - 1 (BD)

3. **Psyllium husk** (Isphaghol)
0 - 0 - 1 (HS)

If Epigastric discomfort/pain

4. **Cap. Omeprazole 40mg** (Risek, Zoltar)
1 - 0 - 0 (OD)

کھانے سے 30 منٹ پہلے



EMERGENCY MANAGEMENT OF CONSTIPATION

1. Admit in emergency department
2. Maintain IV line
3. **Send initial investigation:** US whole abdomen, X-ray abdomen erect and supine, CBC, urea, creatinine & electrolytes (U/C/E).
4. **Inj. Drotaverine 40mg** (Nospa) diluted in 100ml 0.9% NS x IV
5. **Inj. Ketorolac 30mg** (Toradol) dilute in 4-8 ml 0.9% NS x IV slow
6. Correction of electrolytes imbalance
7. Rule out intestinal (obstruction)/rectal pathology first
8. Enema of Sodium Biphosphate 19.2g + Sodium Phosphate 7.2g (**Kleen Enema, Fleet Enema**) → Works by increasing water in the intestine to hydrate and soften the stool and help produce a bowel movement without pain or spasm.
 - » Apply Fleet or Kleen Enema solution rectally while lying down on your **left side position** or in a **knee-chest position**.
 - » Applicator tips for Kleen Enema are lubricated with petroleum jelly for ease of insertion into the rectum.
 - » Attempt to hold the enema solution until the urge to evacuate is strong, but no longer than 10 minutes.

Note: Do not force the enema tip into rectum as this can cause injury





APPROACH TO THE JAUNDICE & CHOLESTASIS

Name:	Age:	Sex:	Date:
Temperature:	B.P:	Pulse:	Resp. Rate:

Jaundice (icterus) is a yellowish discoloration of tissue (skin and the sclera) caused by the accumulation of bilirubin deposits. Jaundice is usually detectable clinically when the serum bilirubin exceeds ≥ 2.5 mg/dL (40 $\mu\text{mol/L}$) term as "Hyperbilirubinemia". Normal - Serum total bilirubin = 0.2–1.2 mg/dL (3.42–20.52 $\mu\text{mol/L}$).

Cholestasis: Impaired production, secretion, or outflow of bile.

ETIOLOGICAL CLASSIFICATION OF JAUNDICE

- Pre-hepatic jaundice:** It is characterized by unconjugated hyperbilirubinemia (predominantly indirect bilirubin) most commonly caused by increased hemoglobin breakdown.
 - » **Hemolysis:** G6PD deficiency, sickle cell anemia, hereditary spherocytosis, autoimmune hemolytic anemia, hemolytic transfusion reaction, erythroblastic fetalis.
 - » **Ineffective erythropoiesis:** Thalassemia, Pernicious anemia, Sideroblastic anemia.
 - » **Increased bilirubin production:** Massive blood transfusions, superficial & internal hematoma resorption.
 - » **Medication side effect (impaired hepatic uptake of bilirubin):** Rifampicin, Probenecid, Ribavirin, anti-malarial drugs, Dapsone, Quinolones, Aspirin, Nitrofurantoin & Protease inhibitors (atazanavir, indinavir)
- Hepatic jaundice:** It can vary from unconjugated hyperbilirubinemia to conjugated hyperbilirubinemia to a combination (Mixed unconjugated and conjugated hyperbilirubinemia) based on the etiology.
 - » **Unconjugated hyperbilirubinemia → Impaired bilirubin conjugation:** Gilbert & Crigler-Najjar syndrome
 - » **Conjugated hyperbilirubinemia:**
 - **Impaired hepatic excretion of bilirubin:** Dubin-Johnson syndrome, Rotor syndrome
 - **Intrahepatic cholestasis:**
 - ↳ **Intrahepatic biliary tract disorders:** Primary biliary cholangitis, primary sclerosing cholangitis, vanishing bile duct syndrome, postoperative cholestasis
 - ↳ **Infiltrative disease:** Tuberculosis, sarcoidosis, amyloidosis, lymphoma
 - ↳ **Pathogenic variant in genes coding for bile salt transport proteins:** Progressive familial intrahepatic cholestasis, benign recurrent intrahepatic cholestasis and some cases of intrahepatic cholestasis of pregnancy
 - ↳ Total parenteral nutrition and Non-hepatobiliary sepsis
 - ↳ **Infectious diseases:** Malaria, icteric leptospirosis, infectious mononucleosis.
 - » **Mixed unconjugated and conjugated hyperbilirubinemia (due to hepatocellular injury):**
 - **Viral hepatitis:** Hepatitis A, B, C, D & E, EBV, CMV, yellow fever
 - **Liver disease:** Alcoholic hepatitis, nonalcoholic steatohepatitis, cirrhosis, congestive hepatopathy, Wilson disease, autoimmune hepatitis
 - **Medications toxicity:** Acetaminophen, estrogens, macrolides, arsenic
- Post-hepatic jaundice:** It is characterized by conjugated hyperbilirubinemia (predominantly direct bilirubin) caused by extrahepatic cholestasis from biliary obstruction.
 - » **Malignancy:** bile duct cholangiocarcinoma, pancreatic cancer, liver cancer, gallbladder cancer, ampullary cancer and liver metastases.
 - » **Gallbladder and gallstone disease:** cholelithiasis, choledocholithiasis, cholangitis, postoperative bile leaks or biliary strictures, Mirizzi syndrome, IgG4 cholangitis, ischemic cholangiopathy, COVID cholangiopathy
 - » **Inflammatory processes:** Primary sclerosing cholangitis, Pancreatitis (acute and chronic)
 - » **Infection:** AIDS cholangiopathy, Liver flukes, Ascariasis

CLINICAL FEATURES

- » **Jaundice**
 - » Scleral icterus (yellow discoloration of the sclerae) develops at serum bilirubin levels $> 2-3$ mg/dL.
 - » Skin discoloration becomes apparent at serum bilirubin levels $> 4-5$ mg/dL.
- » **Pre-hepatic jaundice:**
 - » Jaundice (mild) – lemon yellow discoloration
 - » **Features of anemia due with hemolysis:** Pallor, fatigue, exertional dyspnea, palpitations
 - » Normal color of stool and urine color
 - » Splenomegaly occurs in all hemolytic disorders except in sickle cell disease.
- » **Hepatic jaundice:**
 - » Jaundice (variable) – orange yellow discoloration
 - » Low grade fever, malaise anorexia, fatigue, nausea and vomiting
 - » Right upper quadrant (RUQ) abdominal pain
 - » Tender hepatomegaly
- » **Post-hepatic jaundice (Biliary obstruction):** vary depending on the underlying etiology
 - » **Early features of cholestasis:**
 - » Jaundice (Deep) – Green yellow discoloration
 - » Right upper quadrant (RUQ) abdominal pain
 - » Pruritus (itching sensation of the skin due to deposition of bile salts in the skin)
 - » Pale, clay-colored stool (light-colored stools) due to absence of stercobilin (brown pigments in feces)
 - » Darkening of urine
 - » **Late features of cholestasis:**
 - » **Features of malabsorption (vitamins A, D, E & K):** Weight loss, Steatorrhea (condition of foul-smelling, bulky, oily, floating stool), osteomalacia, bleeding tendency
 - » Xanthelasma on eye lids and xanthomas over tendons due to lipid deposits.
 - » **Features associated with severity, and chronicity of liver dysfunction:** scratch marks, palmar erythema, spider telangiectasias, ascites, gynecomastia, sparse body hair, fetor hepaticus, & asterixis may be present
 - » **Features in biliary obstruction** may be intermittent if caused by a stone or malignancy.
 - » Chronic biliary obstruction leading to backflow of bile may result in inflammation and hepatomegaly.
 - » Pain may be absent early in pancreatic cancer.
 - » **Occult blood in the stools:** suggests cancer of the ampulla.
 - » **Palpable gallbladder (Courvoisier sign/law):** that suggest jaundice is due to a malignant biliary obstruction e.g. characteristic sign of a pancreatic head cancer.
 - » Fever and chills are more common in benign obstruction with associated cholangitis and characterized by 'Charcot's triad' of jaundice, right upper quadrant pain and fever

APPROACH TO PATIENT WITH JAUNDICE

- » **Workup should be done in all patients**
 - » Perform a detailed history taking (including medication history) to identify features of cholestasis, hemolysis, or liver disease.
 - » Perform abdominal examination and assess for hepatomegaly and identify RUQ pain.
 - » **Obtain liver function tests (LFTs)** including total, direct and indirect bilirubin, ALP, GGT
 - » **Obtain other routine laboratory test:** CBC, Urea, creatinine, electrolytes, coagulation profile & urinalysis
 - » **Ultrasound abdomen:** Initial done in all patients with jaundice. Preferred for suspected cholestasis.
- » **Predominant elevation of indirect bilirubin elevation:**
 - » **Obtain a hemolysis workup:** Reticulocytes $\uparrow$, Indirect bilirubin $\uparrow$, LDH $\uparrow$, haptoglobin $\downarrow$, hemoglobinuria, urinary urobilinogen $\uparrow$, and peripheral blood smear shows – schistocytes
 - » Consider specialized testing for hereditary conditions in select cases
- » **Predominant elevation of direct bilirubin**
 - » Distinguish between hepatocellular injury and cholestasis
 - » Obtain additional laboratory studies and radiological imaging

CLINICAL FEATURES & LAB INTERPRETATION USEFUL IN DIFFERENTIATING DIFFERENT TYPES OF JAUNDICE

Features		Pre-hepatic (hemolysis)	Hepatic (hepatocellular)	Post-hepatic (obstructive)
Jaundice		Mild	Variable	Deep
Pruritis		—	Variable	+
Bleeding tendency		—	+	+ (late presentation)
Anemia		+	—	—
Splenomegaly		+	Variable	Absent or later in cirrhosis
Palpable gallbladder		—	—	May be present
Features of cholestasis		—	+ Early presentation	+ Late presentation
Indirect bilirubin		↑↑	↑	Normal
Direct bilirubin		Normal	↑	↑↑
Transaminases: AST, ALT		Normal	↑	Normal
Cholestatic markers: ALP, GGT		Normal	↑	↑↑
PT		Normal	↑↑	↑
APTT		Normal	↑↑	Normal
Albumin		Normal	↓↓	Normal
Urinalysis	Urine color	Normal, Dark urine in Hemoglobinuria	Dark urine	Very dark urine
	Urine bilirubin	Normal	↑	↑↑
	Urine Urobilinogen	↑↑	Normal or ↑	↓
Stool color		Dark	Dark, pale, clay-colored	Pale, clay-colored

Radiological Investigation

1. Initially – Ultrasound abdomen – Findings in abdominal ultrasound include the following

Pre-hepatic jaundice	» Bile ducts with a normal appearance
	» Possible hepatomegaly in conditions causing hemolysis (e.g., malaria, thalassemia)
Hepatic jaundice	» Hepatocellular causes: 1. Cirrhosis (surface nodularity, portal hypertension, ascites) and 2. viral hepatitis (hepatomegaly)
	» Intrahepatic cholestasis: dilated intrahepatic bile ducts, double-barrel shotgun sign
Post-hepatic jaundice	» Dilated common bile duct, double-duct sign
	» Demonstrate of causes of obstruction: e.g., gallstones, malignancy, or cysts

2. CT abdomen with IV contrast (90–95% sensitivity) or MRI abdomen

- » CT/MRI Findings: depend on the etiology
 - » **Hepatocellular injury:** Fibrotic changes, cirrhosis (e.g., nodular surface), general hepatic inflammation
 - » **Cholestasis,** Dilated bile ducts, hepatomegaly and portal hypertension.
 - » **Demonstrate causes of obstruction:** e.g., stones, masses (intrahepatic tumors)
- » **MRI abdomen is the most accurate technique** for identifying isolated liver lesions such as hemangiomas, focal nodular hyperplasia, or focal fatty infiltration and for detecting hepatic iron overload.

3. **Magnetic resonance cholangiopancreatography (MRCP):** It is a sensitive, noninvasive method of detecting bile duct stones, strictures, and dilatation; however, it is less reliable than endoscopic retrograde cholangiopancreatography (ERCP) for distinguishing malignant from benign strictures

4. **Diagnostic procedures:** Depending on clinical suspicion, and in consultation with a specialist, additional diagnostic procedures may be necessary, including:

- » **Endoscopic retrograde cholangiopancreatography (ERCP):** ERCP requires a skilled endoscopist and may be used to demonstrate pancreatic or ampullary causes of jaundice, carry out sphincterotomy and stone extraction, insert a stent through an obstructing lesion, or facilitate direct cholangiopancreatography.
- » **Percutaneous transhepatic cholangiography:** An alternative to evaluating the anatomy of the biliary tract.
- » **Endoscopic ultrasonography (EUS):** It is the most sensitive test for detecting small lesions of the ampulla or pancreatic head and for detecting portal vein invasion by pancreatic cancer. It is also accurate for detecting or excluding bile duct stones.
- » **Percutaneous liver biopsy:** It is considered the definitive study for determining the cause and histologic severity of hepatocellular dysfunction or infiltrative liver disease, although it is subject to sampling error. It is generally performed under ultrasound or, in some patients with suspected metastatic disease or a hepatic mass, CT guidance.



HEPATITIS-A VIRUS (HAV)

Name: _____ Age: _____ Sex: _____ Date: _____
 Temperature: _____ B.P: _____ Pulse: _____ Resp. Rate: _____

- ☛ **Hepatitis-A** is a viral disease caused by the hepatotropic hepatitis-A virus (HAV). HAV infection can cause acute viral hepatitis, which initially manifests with prodromal symptoms, followed by jaundice.
- ☛ **Transmission:** It is transmitted by the fecal-oral route by either person-to-person contact or ingestion of contaminated food or water, and its spread is favored by crowding and poor sanitation.
- ☛ **Incubation period:** 2–6 weeks (average 30 days)

Clinical features

- ☛ **Common symptoms**
- » **Initial non-specific prodromal phase (1-2 weeks):** The onset may be abrupt or insidious, malaise, fatigue, myalgia, arthralgia, poor appetite, right upper quadrant (RUQ) pain, nausea, vomiting and diarrhea usually precedes the development of jaundice by a few days to = 2 weeks (Icteric phase)
 - » **Icteric phase (=2 weeks):** Jaundice, Dark urine and pale stools and Pruritus
- ☛ **Physical exam:** Jaundice, scleral icterus, tender liver, tender splenomegaly, RUQ abdominal tenderness

Diagnostic workup

- ☛ **Initial laboratory investigation**
- » **CBC:** anemia, thrombocytopenia, leukocytosis and leukopenia
 - » **Liver function tests (LFTs):**
 - ☛ **AST & ALT:** ↑ (AST/ALT ratio is usually < 1)
 - ☛ **Total bilirubin:** ↑
 - ☛ **Cholestatic markers:** ALP ↑ & GGT ↑
 - » **Urinalysis:** urine bilirubin ↑, proteinuria
- ☛ **Confirmatory blood testing**
- » **Anti-HAV IgM antibodies:** ↑
 - ☛ Present in patients with active infection
 - ☛ Usually detectable 5–10 days after exposure and 5–10 days before clinical symptoms develop
 - ☛ Levels peak commonly = 1 month after infection. May persist for up to 6 months after infection
 - » **Anti-HAV IgG antibodies:** ↑
 - ☛ Develop during active infection and persist indefinitely after infection or vaccination.
 - ☛ Production begins within 2–3 weeks of infection.
 - » **HAV RNA** can be detected in stool and serum samples using PCR
 - » **Additional testing to rule out other types of hepatitis:** Serum HBsAg and serum AntiHCV
- ☛ **Radiological investigation:** Ultrasound abdomen

Rx

Treatment of Hepatitis-A virus infection

See "Emergency medicine section" = acute hepatitis viral infection

- ☛ Infection is best prevented by improving social conditions, especially overcrowding and poor sanitation.
- ☛ Strict isolation of patients is not necessary, but hand washing after bowel movements is required. Unvaccinated persons who are exposed to HAV are advised to receive post-exposure prophylaxis with a single dose of HAV vaccine or immune globulin (0.01 mL/kg), or both, within 2 weeks of exposure.
- ☛ Bed rest is recommended only if symptoms are marked.
- ☛ If nausea and vomiting or if oral intake is substantially decreased, intravenous 10% glucose is indicated.
- ☛ Strenuous physical exertion, alcohol, and hepatotoxic agents should be avoided. Small doses of oxazepam are safe because metabolism is not hepatic; morphine sulfate should be avoided. Corticosteroids have no benefit in patients with viral hepatitis, including those with acute liver failure.
- ☛ There is no role for antiviral drugs in the therapy of HAV infection.

CHRONIC HEPATITIS-B VIRAL (HBV) INFECTION (2018 AASLD, 2017 EASL)

Introduction: Chronic HBV infections are defined as infections persisting for **MORE THAN 6 MONTHS** with DETECTION OF HBSAG and POSSIBLY SYMPTOMS OF LIVER DAMAGE.

Etiology: Hepatitis B virus (HBV), member of the Hepadnavirus family, circular, double-stranded DNA virus

Transmission:

- » **Sexual:** transmitted when bodily fluids come in contact with broken skin or mucous membranes (mouth, genitals, or rectum)
- » **Parenteral:** due to contaminated needles or instruments that come into contact with the patient blood.
- » **Perinatal/vertical transmission** → **Mother-to-child-transmission**
- » **Common associations:** HCV and HIV-positive individuals, Travelers to regions where HBV is endemic

Overview Diagnostically relevant virus antigens and antibodies

HBV antigen	Description	Corresponding antibodies
HBsAg (Hepatitis-B surface antigen)	» Protein on the surface of HBV » First evidence of infection » Continued presence indicates a carrier state	Anti-HBs » Without HBsAg, Anti-HBs indicates immunity to HBV due to resolved infection or vaccination » Usually appears ~ 1–3 months after infection or vaccination
HBcAg (Hepatitis-B core antigen)	» Protein of the nucleocapsid » Not routinely measured in clinical practice	Anti-HBc » Anti-HBc IgM: indicates recent infection with hepatitis B (≤ 6 months) » Anti-HBc IgG: indicates resolved or chronic infection
HBeAg (Hepatitis-B envelope antigen)	» Protein secreted by infected hepatocytes into the bloodstream » Indicates active viral replication and thus highly infectious and a poor prognosis	Anti-HBe: indicates long-term clearance of HBV and thus low transmissibility

Common serologic patterns in hepatitis B virus (HBV) infection and their interpretation

HBsAg	Anti-HBs	Anti-HBc	HBeAg	Anti-HBe	Interpretation
+	–	↑ IgM	+	–	Acute HBV infection, ↑ (ALT > AST)
–	–	↑ IgM, followed by ↑ IgG	–	– or ↑	Window period, ↑ (ALT > AST)
–	+	↑ IgG	–	– or ↑	Recovery from Hepatitis-B (immunity)
+	–	↑ IgG	+	–	Active chronic infection (high transmissibility) HBV DNA > 2000 IU/mL
+	–	↑ IgG	–	+	Inactive chronic infection (low transmissibility) HBV DNA $\leq$ 2000 IU/mL
–	+	–	–	–	Vaccination (immunity)
–	–	↑ IgG	–	–	False-positive; less commonly, infection in remote past

INDICATION FOR INITIATING ANTIVIRAL TREATMENT IN CHRONIC HEPATITIS B INFECTIONS

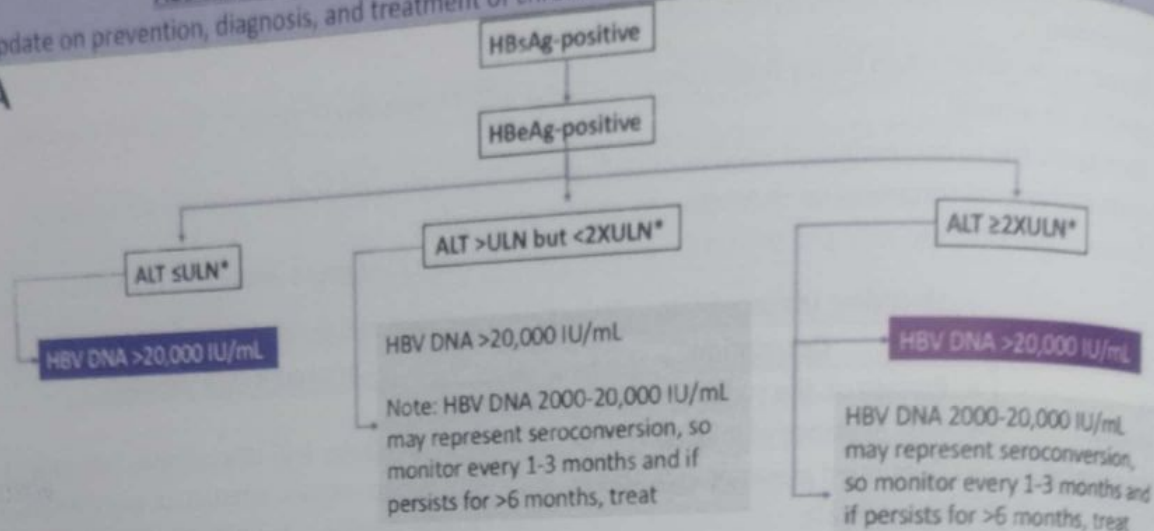
1. Cirrhosis or advance liver fibrosis
2. Acute liver failure
3. **Immune active phase:** ALT $\geq 2 \times$ UNL PLUS significantly elevated HBV DNA levels or without HBeAg
4. **HBV reactivation:** an increase in HBV DNA or change from HBsAg negative to HBsAg positive in anti-HBc-positive patients' immune suppression in HBV positive patients.
5. Co-infection with HCV or HIV
6. Family history of Hepatocellular carcinoma (HCC)

❖ N.B. antiviral therapy is generally not indicated in acute HBV (< 6 months infections), instead, patients with they are typically monitored closely for any signs of complications or progression to chronic HBV.

ALGORITHM FOR MANAGEMENT OF CHRONIC HEPATITIS B VIRAL INFECTION

(Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis-B guidance)

A



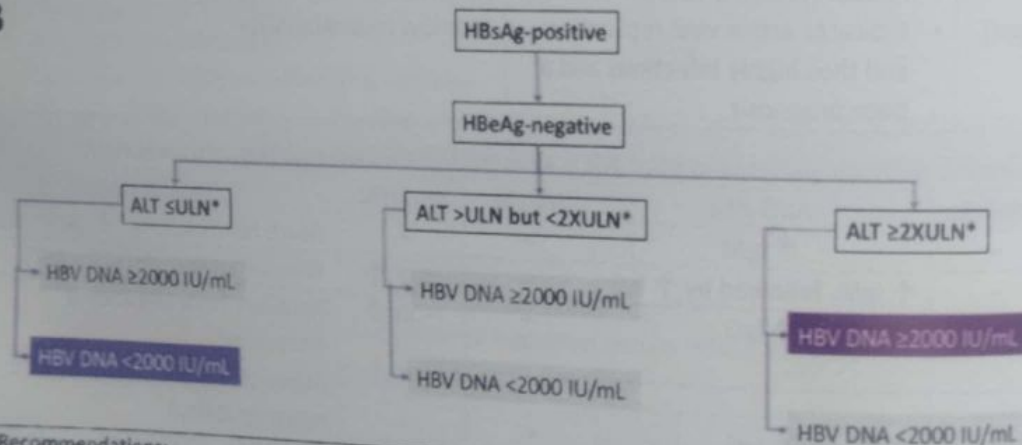
Recommendations:

Treat

Do not treat. Monitor with ALT and HBV DNA levels every 3-6 months and HBeAg every 6-12 months.

Exclude other causes of ALT elevation and assess disease severity with non-invasive tests and/or liver biopsy. If staging indicates ≥ F2 or ≥ A3, treat. If other causes of ALT > ULN excluded and elevation persists, treat, especially if age > 40.

B



Recommendations:

Treat

Do not treat. Monitor with ALT and HBV DNA levels every 3-6 months and HBsAg annually.

If ALT ≤ ULN, monitor ALT and HBV DNA every 3 months for 1 year, then every 6 months. If ALT elevated, exclude other causes of ALT elevation and assess disease severity with non-invasive tests and/or liver biopsy. If staging indicates ≥ F2 or ≥ A3, treat. If persistent ALT > ULN with HBV DNA ≥ 2000 IU/mL, treat, especially if age > 40.

*The upper limits of normal for ALT in healthy adults is reported to be 29 to 33 U/L for males and 19 to 25 U/L for females. An upper limit of normal for ALT of 25 U/L for males and 25 U/L for females is recommended to guide management decisions.

Algorithm for management of HBsAg-positive persons without cirrhosis who are HBeAg-positive (A) or HBeAg-negative (B). *The upper limits of normal (ULN) for ALT in healthy adults are reported to be 29-33 U/L for males and 19-25 U/L for females. An upper limit of normal (ULN) for ALT of 35 U/L for males and 25 U/L for females is recommended to guide management decisions.

Reference:

- 1. <https://aasldpubs.onlinelibrary.wiley.com/doi/10.1002/hep.29800>
- 2. <https://www.aasld.org/practice-guidelines/chronic-hepatitis-b>

SUMMARY OF DIFFERENT GUIDELINES FOR TREATMENT OF CHRONIC HEPATITIS B VIRUS INFECTION

- ❖ N.B. THERE IS NO CURE FOR HEPATITIS B VIRUS (HBV) INFECTION, ONLY CONTROL.
TREATMENT AIMS IS IMMUNOLOGIC CURE (THAT IS CLEARANCE OF HBSAG AND SUSTAINED HBV DNA SUPPRESSION) AND REDUCTION OF LIVER-RELATED COMPLICATION, MORBIDITY AND MORTALITY.
1. World Health Organization (WHO) 2015 Guidelines
 - ☛ When to initiate treatment: Compensated or decompensated cirrhosis (or APRI > 2 in adults), Age >30 years, persistently abnormal ALT, and HBV DNA > 20,000 IU/ml HBV DNA not available, then on bases of persistently abnormal ALT levels
 - ☛ What to treat with: Tab. Entecavir or Tab. Tenofovir disoproxil
 - ☛ When to stop treatment: Lifelong treatment in cirrhosis, Stop treatment if non-cirrhotic, HBeAg seroconversion, or persistently normal ALT levels with or without undetectable HBV DNA, Stop treatment in case of persistent HBsAg loss with 1 year of consolidation therapy
 - ☛ Retreatment: Reactivation of HBV
 2. American Treatment Association (ATA) 2015 Guidelines
 - ☛ When to initiate treatment: ALT level >2 x ULN (upper limits of normal) and HBV DNA >2,000 IU/ml, Compensated/decompensated cirrhosis with detectable HBV DNA
 - ☛ What to treat with: Tab. Entecavir or Tab. Tenofovir disoproxil or Inj. Peg IFN- α
 - ☛ When to stop treatment: HBsAg loss for 6–12 months
 - ☛ Retreatment: Relapse of HBV with respect to HBV DNA and ALT levels (specific levels not provided)
 3. Asia-Pacific Association for the Study of Liver (APASL) 2015 Guidelines
 - ☛ When to initiate treatment: ALT >2 x ULN and HBV DNA >2,000 IU/ml in HBeAg negative or >2,000 IU/ml in HBeAg-positive, Compensated or decompensated cirrhosis with detectable HBV DNA
 - ☛ What to treat with: Tab. Entecavir or Tab. Tenofovir disoproxil or Inj. Peg interferon-alpha (Inj. Peg IFN- α) or Tab. Lamivudine, or Less preferred drugs are Tab. Adefovir or Tab. Telbivudine
 - ☛ When to stop treatment: HBsAg loss for at least 12 months Non-cirrhotic HBeAg seroconversion and undetectable HBV DNA after minimum 1 yr (preferably 3 yr) of consolidation therapy, Non-cirrhotic HBeAg negative and undetectable HBV DNA for ≥ 2 year
 - ☛ Retreatment: None
 4. European Association for the Study of Liver (EASL) 2017 Guidelines
 - ☛ When to initiate treatment: HBV DNA >2,000 IU/ml, ALT >ULN and moderate liver necro-inflammation or fibrosis (F2 minimum), Compensated or decompensated cirrhosis with detectable HBV DNA, HBV DNA >20,000 IU/ml and ALT ≥ 2 x ULN, HBeAg positive, high HBV DNA level, and age 30 years, Family history of HCC, cirrhosis, extrahepatic manifestations
 - ☛ What to treat with: Tab. Entecavir or Tenofovir disoproxil or Tenofovir alafenamide or Inj. Peg IFN- α
 - ☛ When to stop treatment: HBsAg loss Non-cirrhotic HBeAg positive with seroconversion and undetectable HBV DNA after 12 months of consolidation therapy, Noncirrhotic HBeAg negative with undetectable HBV DNA for 3 year
 - ☛ Retreatment: Similar to treatment-naive patients
 5. American Association for the Study of Liver Diseases (AASLD) 2018 Guidelines
 - ☛ When to initiate treatment: ALT >2 x ULN (upper limits of normal) and HBV DNA >2,000 IU/ml in HBeAg negative or > 20,000 IU/ml in HBeAg positive, Cirrhosis with HBV DNA > 2,000 IU/ml, Age 40 years, family history of HCC, previous treatment, extrahepatic disease
 - ☛ What to treat with: Tab. Entecavir or Tab. Tenofovir disoproxil or Inj. Peg IFN- α
 - ☛ When to stop treatment: Stop when HBsAg loss, Lifelong in cirrhosis
 - ☛ Retreatment: None



△ Chronic HBV Infection C/C:

- » Most patients are inactive, non-contagious carriers.
- » Potential reactivation of chronic inactive hepatitis can manifest variably in the following ways:
 - » Asymptomatic
 - » Unspecific symptoms
 - Fatigue, malaise
 - Nausea, poor appetite
 - Unspecific abdominal pain
 - Similar to acute hepatitis
 - Hepatic failure

Treatment duration: 48 weeks or more

Specific Investigation

- » Screening: send HBsAg & anti-HBc IgM
- » If HBsAg is positive: measure HBeAg & HBV DNA to determine transmissibility

Investigation for additional evaluations

- » CBC may show anemia
- » LFTs, Albumin, ChE, coagulation test

↳ Chronic hepatitis

- High variability: mildly ↑ or unchanged AST & ALT
- AST & ALT: AST/ALT ratio ≥ 1
- GGT: ↑

↳ Cirrhosis

- Serum albumin: ↓
- Coagulation profile: ↑ INR/PT
- Bilirubin: ↑
- Serum cholinesterase (ChE): ↓

Note: Serum ChE is an excellent biomarker of cirrhosis with good sensitivity & specificity. It shows good correlation with serum albumin, PT INR and MELD score. Since it distinguishes Decompensated cirrhosis from compensated cirrhosis well, low levels in cirrhosis may serve as a useful prognostic marker of advanced liver disease.

Test of common coinfections: Coinfection with hepatitis C, hepatitis D, syphilis, and HIV (↓ CD4 count) is common and should be tested for accordingly.

Ultrasound abdomen:

- » Decreases echogenicity and number of portal vein radicle walls
- » Increases Liver echogenicity

Acute hepatitis-D infection superimposed on chronic HBV infection may result in severe chronic hepatitis, which may progress rapidly to cirrhosis and may be fatal. Patients with long-standing chronic hepatitis-D and B often have inactive cirrhosis and are at risk for decompensation and hepatocellular carcinoma. The diagnosis is confirmed by detection of anti-HDV or HDAg (or HDV RNA) in serum.

TREATMENT OF CHRONIC HBV INFECTION

Rx

» Lifestyle changes

- » Weight loss
- » Cessation of substance use (including alcohol)
- » Discontinuation of hepatotoxic medication

1. Tab. Entecavir (ETV) 0.5mg (Ecavir, Tacavir) (Tenofo-B, Hilfovir, Gentovir, Vireof)

OR Tab. Tenofovir Disoproxil (TDF) 300mg

OR Tab. Tenofovir Alafenamide (TAF) 25mg (Tefod, Tenofovir-AF)
0-0-1 (OD)

» If Patient resistance to ETV, Switch to TDF or TAF

» If patient is multidrug resistance, Switch to ETV PLUS TDF or TAF combination (EASL 2017)

Supportive treatment:

2. Consider: Tab. L-Methylefolate 400mcg (Myfol, Maxfol, Folate) 0-0-1 (OD)

3. For constipation: Syp. Lactulose (Duphalac, Lilac) 0-0-30ml x HS

4. For epigastric upset: Cap. Esomeprazole 40mg (Nexum, Esoq) 1-0-0 (OD)

کھانے سے 30 منٹ پہلے

N.B.

» **Nucleoside/Nucleotide Analogs:** indicated for patients with both decompensated & compensated liver disease and nonresponders to interferon treatment: Entecavir or Tenofovir (DOC)

» **Pegylated interferon alfa (PEG-IFN-α):** especially in younger patients with compensated liver disease

» Regimen is shorter than nucleoside/nucleotide analogs

» **Contraindications:** Decompensated cirrhosis, Psychiatric conditions, Autoimmune conditions, Pregnancy and Leukopenia or thrombocytopenia

» Coinfection with HDV is best treated with PEG-IFN-α

» **Hepatitis B in pregnancy:** Tenofovir (DOC), Lamivudine, & Telbivudine (PEG-IFN-α is contraindicated during pregnancy)

» Liver biopsy

A biopsy is indicated in the following cases:

- » Diagnosis is uncertain.
- » Exclusion of other possible causes of liver damage in chronic disease or severely affected individuals
- » Assessment of disease severity in patients with active CLD (i.e., ↑ AST/ALT and detectable levels of HBV DNA)

» Liver transplantation

- » In cases of end-stage liver disease due to HBV
- » In cases of fulminant hepatic failure (emergent transplantation)

CHRONIC HEPATITIS-C VIRAL (HCV) INFECTION

Name: _____ Age: _____ Sex: _____ Date: _____
Temperature: _____ B.P: _____ Pulse: _____ Resp. Rate: _____

Introduction: Chronic HCV infections are defined as infections persisting for **MORE THAN 6 MONTHS WITH DETECTION OF ANTI-HCV** following exposure and possibly symptoms of liver damage.

Etiology: Hepatitis-C virus (HCV) → RNA virus of the Hepacivirus genus and Flaviviridae family

Transmission:

- » Parenteral: Needle sharing among individuals who use injection drugs, needlestick injury (health care workers), blood transfusion and dialysis
- » Organ transplantation
- » Perinatal/vertical transmission → Mother-to-child-transmission
- » Sexual: rare (in contrast to HBV and HIV)
- » Common risk factor: Hepatitis-B virus (HBV) and HIV-positive individuals, Injection drug use (especially long-term use) and History of incarceration

Clinical features

Incubation period: 2 weeks to 6 months

Acute course features

- » Asymptomatic in 80% of cases
- » Symptomatic
 - ↳ Malaise, fever, myalgias, arthralgias
 - ↳ Right upper quadrant (RUQ) abdominal pain
 - ↳ Tender hepatomegaly
 - ↳ Nausea, vomiting, diarrhea
 - ↳ Jaundice, possibly pruritus

Chronic course features

- » Seen especially in asymptomatic individuals (up to 85%), as the disease may go undiagnosed and treatment may be delayed or never initiated (carrier state).
- » Findings often mild, nonspecific (e.g., fatigue)
- » Liver cirrhosis (up to 25% of cases) within 20 years of infection
- » Extra-hepatic features (common)
 - ↳ Hematological system
 - Mixed cryoglobulinemia
 - Lymphoma (especially B-cell non-Hodgkin lymphoma)
 - Immune thrombotic thrombocytopenia (ITP)
 - Autoimmune hemolytic anemia
 - Monoclonal gammopathies
 - ↳ Renal system
 - Membranoproliferative glomerulonephritis (more common)
 - Membranous glomerulonephritis
 - ↳ Rheumatological
 - Polyarteritis nodosa
 - Sjogren syndrome
 - ↳ Dermatological
 - Porphyria cutanea tarda
 - Lichen planus
 - ↳ Endocrinal system
 - Diabetes mellitus
 - Autoimmune thyroiditis (may lead to hypothyroidism)
 - ↳ Vascular: Leukocytoclastic vasculitis
 - ↳ Sialadenitis: inflammation of the salivary gland.

Treatment duration: 8-12 weeks or more

Specific Investigation

- » Initial screening test: send serum anti-HCV antibodies (by EIA/ELISA immunoassay)
- » If Anti-HCV antibody test is positive
Send → HCV RNA PCR (Qualitative)

Additional evaluations → Test obtain before treatment to exclude liver cirrhosis and its complications and assess for comorbidities.

- » **Viral load determination:** quantitative PCR for HCV RNA
- » **Routine blood test**
 - » CBC: may show anemia
 - » BUN and serum creatinine
 - » Serum electrolytes
- » **LFTs, serum albumin, GGT, PT & INR**
 - » **Hepatocellular enzyme**
 - AST/ALT: mildly ↑
Or normal (10 - 20 x ULN)
 - Fluctuating ALT peaks indicate acute HCV infection
 - » **Cholestasis parameters**
 - GGT: ↑
 - Alkaline phosphatase (ALP): ↑
 - Bilirubin: ↑
 - » **To rule out cirrhosis**
 - Albumin: ↓
 - Total protein: ↓
 - Coagulation profile: PT, INR ↑
 - Bilirubin: ↑
 - » **Evaluation of coinfection**
 - HIV: HIV serological assay
 - Hepatitis-B: Serum HBsAg
 - Hepatitis-A: Anti-HAV IgM & IgG
 - » **In female** → Serum pregnancy test (if applicable) ideally performed directly before initiating treatment
 - » **Ultrasound whole abdomen**

Monitoring: HCV is curative, the definition of clearance of HCV RNA requires use of a sensitive real-time reverse transcriptase-PCR assay to monitor HCV RNA during treatment (the lower limit of quantification should be 25 IU/mL or less, and the limit of detection should be 10-15 IU/mL).

Rx

Prescription #1

1. Cap. Sofosbuvir 400mg (Sofomac, Sofohil, Sofiget)
0-0-1 (OD)
2. Cap. Daclatasvir 60mg (Maclinza, Clavir, Daclaget)
0-0-1 (OD)

HCV with Cirrhosis add on

3. Cap. Ribavirin 400mg (Viron, Novia, Ribazole)
0-0-1 (OD)

Supportive treatment:

4. Consider: Tab. L-Methylefolate 400mcg (Myfol, Maxfol)
0-0-1 (OD)
5. For constipation: Syp. Lactulose (Duphalac, Lilac)
0-0-30ml x HS
6. For epigastric upset: Cap. Esomeprazole 40mg (Esso)
1-0-0 (OD)
کھانے سے 30 منٹ پہلے

Rx

Prescription #2

(Maclusa, Hilvel, Velpaget, Eplusa)

1. Cap. Sofosbuvir 400mg + Velpatasvir 100mg
» Not recommended in patients with compensated cirrhosis with HCV genotype-3
(Syneget-LS, Sofopas, Harvoni)
OR Cap. Sofosbuvir 400mg + Ledipasvir 90mg
Cap. Glecaprevir 100mg + Pibrentasvir 40mg (Mavyret)
0-0-1 (OD)
2. Tab. L-Methylefolate 400mcg (Myfol, Maxfol, Folate)
0-0-1 (OD)

- » **Drug interactions:** Certain cytochrome P450/ P-glycoprotein inducing medications, such as carbamazepine, phenytoin, and phenobarbital, contraindicate the use of all HCV direct-acting antiviral regimens.
- » **HCV infection is easy to cure with oral direct-acting agents, with expected sustained virologic response rates well above 90%.**
- » **HCV with cryoglobulinemia:** Antiviral therapy has been shown to be beneficial in the treatment of cryoglobulinemia associated with chronic hepatitis-C; an acute flare of cryoglobulinemia may first require treatment with rituximab, cyclophosphamide plus methylprednisolone, or plasma exchange.

Preferred FDA-approved oral direct-acting antiviral (DAA) treatment regimens for HCV infection.

Regimen	Indication	Duration of treatment in non-cirrhotic treatment-naïve patients
Glecaprevir + Pibrentasvir	All 6 genotypes	OD for 8 weeks
Sofosbuvir + Velpatasvir	All 6 genotypes	OD for 12 weeks
Sofosbuvir + Ledipasvir	Genotypes 1, 4, 5, and 6	OD for 8-12 weeks
Sofosbuvir + Daclatasvir	Genotypes 1, 3, 4	OD for 12 weeks (24 weeks for cirrhotic)
Sofosbuvir + Velpatasvir + Voxilaprevir	All 6 genotypes	OD for 12 weeks

NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) OR (FATTY LIVER OR HEPATIC STEATOSIS)

△ Fatty liver disease

- C/C:
- » Most patients are asymptomatic
 - » Right upper quadrant (RUQ) discomfort
 - » Abdominal pain
 - » Anorexia and weight loss
 - » Excessive fatigue, malaise
 - » Easy bruising
 - » Hepatomegaly
 - » May progress to cirrhosis

Causes:

- » Obesity
- » Hypertension
- » Diabetes mellitus type-2
- » Excessive cholesterol
- » Hypertriglyceridemia
- » Hepatitis-B and hepatitis C
- » Polycystic ovarian syndrome
- » Endocrinopathies (Cushing's syndrome)
- » Hypothyroidism
- » Medications: amiodarone, glucocorticoids, doxycycline, antiretroviral drugs, estrogen

Diagnostic workup

- » Complete blood count (CBC): may show anemia
- » LFTs: ↑ Transaminases (AST/ALT ratio < 1) the reversal of the AST/ALT ratio to values > 1 may indicate progression to cirrhosis.
- » Fasting lipid profile – (12 hour fasting)
- » Send serum HBsAg and serum Anti-HCV to rule out hepatitis-B (HBV) and hepatitis-C infection (HCV).
- » Ultrasound: Macrovascular steatosis
- » CT scan or MRI: Macrovascular steatosis
- » MRI-proton density fat fraction or magnetic resonance spectroscopy - rule out hepatic fibrosis

Low risk fatty liver disease

- » Fatty changes on ultrasound
- » Normal LFTs
- » Fibroscan normal

High risk fatty liver disease

- » Fatty changes on ultrasound
- » Abnormal LFTs
- » High reading on Fibroscan

NOTE: Studies suggest that ursodeoxycholic acid may have anti-inflammatory & anti-apoptotic effects in the liver, that vitamin-E may ↓ oxidative stress & improve AST levels in NASH patients. There is controversy as to whether vitamin-E ↑ the risk of prostate cancer in men and hemorrhagic stroke (CMDT-2023)

Pathology of Nonalcoholic fatty liver disease (NAFLD)

- » Hepatocellular lipid accumulation, mostly macrovesicular
- » Ballooning degeneration and necrosis
- » Inflammatory infiltrates, with scattered lymphocytes, neutrophils, and Kupffer cells

Pathophysiology Nonalcoholic fatty liver disease (NAFLD):

- » ↑ Insulin resistance
- » ↑ Hepatic uptake of fatty acids
- » ↑ Triglyceride synthesis
- » ↑ Peripheral lipolysis

Rx

Prescription # 1

☞ Lifestyle changes for reduction of fatty liver:

- » Moderate exercise, Gradual weight loss, average of 0.5–1 kg/week (rapid weight loss can worsen liver disease) Aim to lose weight at least 5%–10%
- » Dietary fat restriction

☞ Avoid smoking and alcohol

☞ Discontinue responsible medication

☞ Control of co-morbidities: Diabetes, dyslipidemia

☞ Consider liver transplantation in patients with end-stage liver disease

1. Cap. Vitamin-E 600mg (Evion) x 0 – 0 – 1

2. Cap. Esomeprazole 40mg (Nexum, Esso)
1 – 0 – 0 (OD x 30 minutes before foods)
کھانے سے 30 منٹ پہلے

If triglyceride: ↑ (Ovaza, Omacor, Seamega, Romega)

3. Softgel Cap. Omega-3-acid ethyle esters 90 x BD
OR Tab. Atorvastatin 10mg (Lipiget, Lipitor) x HS
OR Tab. Rosuvastatin 5mg + Ezetimibe 10mg (RolipEze 5/10mg, Rovista Ez 5/10mg) x 0 – 0 – 1 (HS)
Monitor with lipid profile at least 10-12 hour fasting, after 4 weeks, increase the dose if not respond.

Rx

Prescription # 2

1. Lifestyle modification (as mentioned above)

2. Tab. Metformin 500mg (Glucophage, Neophage)
1 – 0 – 1 (BD) – for best in obese/insulin resistant cases
OR Cap. Ursodeoxycholic acid (Cap. Urso 500mg)
Dosage: 12–15 mg/kg/day

3. Cap. Vitamin-E 600mg (Evion) x 0 – 0 – 1

4. Cap. Omeprazole 40mg (Risek, Ruling)
1 – 0 – 0 (OD) x on empty stomach 30min before meals.
کھانے سے 30 منٹ پہلے

ASCITES

Name: _____ Age: _____ Sex: _____ Date: _____
 Temperature: _____ B.P: _____ Pulse: _____ Resp. Rate: _____

ETIOLOGY OF ASCITES

- ☞ The etiology can be determined using the serum-ascites albumin gradient (SAAG) based on Starling's law.
 ☞ $SAAG = (\text{albumin levels in serum}) - (\text{albumin levels in ascitic fluid})$

High SAAG ascites ≥ 1.1 g/dL (obsolete term: Transudate)	Low SAAG ascites < 1.1 g/dL (obsolete term: Exudate)
Portal hypertension ☞ Presinusoidal » Splenic or portal vein thrombosis » Schistosomiasis ☞ Sinusoidal Hepatic (common) » Cirrhosis » Alcohol-related liver disease » Liver metastases ☞ Postsinusoidal » Right heart failure » Constrictive pericarditis » Budd-Chiari syndrome	Hypoalbuminemia ☞ Nephrotic syndrome ☞ Severe malnutrition ☞ Protein-losing enteropathy Malignancy: Peritoneal carcinomatosis, lymphoma, and hepatocellular carcinoma Infections: Tuberculosis - Production of protein-rich fluid from tubercles Pancreatitis: Accumulation of pancreatic fluid in the peritoneal cavity

CLINICAL FEATURES

- » Progressive abdominal distension; symptoms associated with increased abdominal distention include
- Early satiety
 - Weight gain
 - Dyspnea
 - Diarrhea, which, if chronic, may be associated with features of malnutrition
- » **Fluid wave test:** wave produced by tapping one side of the abdomen in a patient in supine position; this wave will be transmitted to the other side via ascitic fluid.
- » **Shifting dullness:** change of resonance from dull to tympanic resonance when patient changes from supine to lateral decubitus position.
- » **Flank dullness:** typically elicited only if > 1.5 L of ascitic fluid is present.
- » Abdominal pain may be present
- » Abdominal wall hernias (e.g., umbilical, inguinal, or incisional hernias)
- » Peripheral or generalized edema
- » **Signs of underlying disease**
- Enlarged liver, jaundice, spider angioma, palmar erythema $\rightarrow$ chronic liver disease
 - Elevated jugular venous pressure $\rightarrow$ heart failure
 - Virchow's node; and weight loss $\rightarrow$ upper abdominal malignancy

SUB-TYPES OF ASCITES

Chylous ascites

- ☞ **Definition:** collection of lymph in the abdominal cavity, which is characteristically triglyceride-rich and has a milky appearance
- ☞ **Etiology:** malignancy (e.g., lymphoma), hepatic cirrhosis, or other lymph disorders (e.g., lymphatic hyperplasia) which result in increased lymph production

Bloody ascites

- ☞ **Definition:** ascitic fluid with $RBC > 50,000$ mm³
- ☞ **Etiology:** may be spontaneous (e.g., due to peritoneal carcinomatosis or a malignant mass eroding into vessels) or iatrogenic (e.g., following paracentesis or biopsy in patients with cirrhosis)

Diagnostic workup

- CBC: Thrombocytopenia, anemia
- Coagulation profile: PT/INR ↑
- LFTs: Abnormal
- Serum albumin: ↓
- Urea, creatinine & electrolytes: deranged
- Initial imaging: Abdominal ultrasound
- CT scan abdomen (and pelvis)
- Diagnostic paracentesis

Diagnostic paracentesis is indicated for all patients who have new ascites or who have been hospitalized for a complication of cirrhosis; it reduces mortality, especially if performed within 12 hours of admission, to identify the underlying etiology – spontaneous bacterial peritonitis (SBP). Repeat large-volume paracentesis (with IV albumin, Haemaccel infusion).

Ascitic fluid analysis:

- **Gross appearance:** can provide supportive evidence of the underlying cause or complications
- **Transparent to yellow:** uncomplicated ascites
- **Cloudy:** infection or malignancy
- **Bloody:** trauma or malignancy
- **Milky:** chylous ascites
- **Dark brown:** suggestive of a biliary leak (e.g., gallbladder perforation)
- **Cell count and differential:** A neutrophil count ≥ 250 cells/mm³ indicates spontaneous bacterial peritonitis (SBP).
- **Ascitic fluid albumin:** for SAAG calculation (obtain same-day serum & ascitic fluid samples)
- **Ascitic fluid total protein**
 - To differentiate cirrhosis from cardiac etiologies in high SAAG ascites
 - To differentiate SBP (typically ≤ 1 g/dL) from secondary peritonitis (typically > 1 g/dL)

Note: Occult spontaneous bacterial peritonitis (SBP) is common in patients with ascites/cirrhosis and delays in diagnosis may lead to mortality.



TREATMENT OF ASCITES

1. **All ascitic patients:** Identify & treat the underlying cause & therapeutic paracentesis for tense or large ascites
2. **Patients with cirrhotic ascites:** Treatment of cirrhosis, avoid medications (NSAIDs, ACEIs) & liver transplant.
3. **Patients with noncirrhotic ascites:** treat underlying cause
 - » Treatment of heart failure
 - » Antituberculosis therapy
 - » Surgery or radiochemotherapy for malignancy

Salt & fluid restriction:

Dietary sodium restriction: 2g/day or 88 mEq/day (2g of sodium = 5g of salt)

- » Recommended for all patients
- » Advise patients to restrict the amount of salt in home-cooked meals and to avoid precooked and prepackaged food.
- » Consider referral to a nutritionist for counselling.

Fluid restriction: 1L/day (only if serum Na⁺ < 125 mEq/L).

Initiate Diuretics

- » **Tab. Spironolactone 100mg** (Aldactone) x at dose 100mg PO once a day; titrate up every 3–5 days as needed (max. dose 400 mg/day)
- » **OR Combination therapy:**
 - » **Tab. Spironolactone 100mg** (Aldactone) 0–0–1 (OD) as dose explained above
 - » **Tab Furosemide 40mg** (Lasix) at dose 40 mg PO once a day; titrate up every 3–5 days as needed (max. dose 160 mg/day). 1–0–1 (BD)
- » Once ascites is under control, taper diuretics to the minimum effective dose to reduce side effects.

Tab. L-methylefolate 400mcg (Myfol, Maxfol) 0–0–1 (OD)

Gastroprotective: Cap. Omeprazole 40mg (Ruling, Risek) 0–0–1 (OD) x کھانے سے 30 منٹ پہلے

With constipation: Syp. Lactulose (Duphalac, Lilac) 0–0–30ml (HS)

With suspected infection/SBP: initiate empiric antibiotics
See surgery section – treatment of SBP

Differential diagnoses of ascites based on SAAG and ascitic fluid total protein

SAAG	Ascites due to portal hypertension	Ascites due to other causes
	» ≥ 1.1 g/dL	» < 1.1 g/dL
Ascitic fluid total protein levels	» ↑ Protein levels (> 2.5 g/dL): Right heart failure » ↓ Protein levels (< 2.5 g/dL): Hepatic cirrhosis	» ↑ Protein levels (> 2.5 g/dL): ▪ Peritoneal carcinomatosis ▪ Pancreatitis ▪ Tuberculosis ▪ Chylous ascites (not secondary to cirrhosis) » ↓ Protein levels (< 2.5 g/dL): Nephrotic syndrome

DECOMPENSATED CHRONIC LIVER DISEASE (DCLD) = LIVER CIRRHOSIS + ASCITES

Name:

Age:

Sex:

Date:

Temperature:

B.P.:

Pulse:

Resp. Rate:

△ DCLD

C/C:

- Fatigue, malaise, weight loss
- Jaundice
- Hematemesis
- Hepatomegaly (possibly causing RUQ pain)
- Splenomegaly
- Ascites

Investigation

- ☞ CBC, U/C/E, LFTs, PT & INR
- ☞ U/S Abdomen, CXR
- ☞ HBsAg and Anti-HCV
- ☞ CT scan abdomen with contrast
- ☞ Total protein serum albumin AG ratio (TPAGR)

Salt and fluid restriction

Dietary sodium restriction: 2g/day or 88 mEq/d (2g of sodium = 5g of salt)

- » Recommended for all patients
- » Advise patients to restrict the amount of salt in home-cooked meals and to avoid precooked and prepackaged food.
- » Consider referral to a nutritionist for counselling.

Fluid restriction: 1 L/day (only if serum Na⁺ < 125 mEq/L).

Combination therapy with spironolactone; PLUS, furosemide in a 10:4 ratio may be preferable for recurrent gross ascites or when faster resolution of ascites is required (e.g., in hospitalized patients).

Diuretics should be used with caution in patients with severe hyponatremia, hepatic encephalopathy, and/or renal function deterioration.

Once ascites is under control, taper to the minimum effective dose to reduce side effects.

Rx

1. Tab. Carvedilol 6.5mg (Carvida, Carlov)
 $\frac{1}{2} + 0 + \frac{1}{2}$ (Half Tablet BD)
 2. Tab. Spironolactone 100mg (Aldactone)
0-0-1 (OD)
OR Tab. Spironolactone 25mg (Aldactone-A) x TDS
 3. Tab Furosemide 20mg or 40mg (Lasix)
1-0-1 (BD)
 4. Tab L-methylefolate 400mcg (Myfol, Maxfol, Folate)
OR Tab Folic acid 5mg
0-0-1 (OD)
 5. Cap Esomeprazole 40mg (Nexum, Esso)
1-0-0 (OD)
کھانے سے 30 منٹ پہلے
- In this case mostly Patient complaint about constipation
If present than treat with
6. Syp Lactulose (Duphalac, Lilac)
0-0-30ml (HS)

Rx

1. Tab. Propranolol 40mg (Inderal, Cardinal)
 $\frac{1}{2} + 0 + \frac{1}{2}$ (Half Tablet BD)
 2. Tab. Spironolactone 20 mg + Furosemide 50mg (Spiromide)
1-0-1 (BD)
 3. Tab. L-methylefolate 400mcg (Myfol, Maxfol, Folate)
OR Tab. Folic acid 5mg
0-0-1 (OD)
 4. Cap. Omeprazole 40mg (Risek, Ruling)
1-0-0 (OD)
کھانے سے 30 منٹ پہلے
- If constipation treat with
5. Syp Lactulose (Duphalac, Lilac)
0-0-30ml (HS)

PRIMARY BILIARY CHOLANGITIS (PBC)

Name: _____ Age: _____ Sex: _____ Date: _____
 Temperature: _____ B.P: _____ Pulse: _____ Resp. Rate: _____

Clinical features

- Patients are initially often asymptomatic for years.
- Signs and symptoms are mainly due to the resulting cholestasis, liver cirrhosis, and portal hypertension.
 - » Insidious onset and is heralded by first symptom – fatigue (excessive daytime somnolence)
 - » Marked generalized pruritus
 - » Hyperpigmentation
 - » Hepatosplenomegaly
 - » Abdominal dull lower margin, right upper quadrants (RUQ) discomfort
 - » Jaundice, steatorrhea, pale stool, dark urine
 - » Maldigestion (deficiency vitamins A,D,E,K)
 - » **Xanthomatous lesions** may occur in the skin and tendons and around the eyelids (xanthelasma).
 - » The risk of low bone density, osteoporosis, & fractures is increased in pt. with PBC (who tend to be older women)
- Frequently associated with other autoimmune conditions:** Rheumatoid arthritis, Autoimmune thyroid disease, especially Hashimoto thyroiditis, Celiac disease, CREST syndrome & Sicca syndrome

Laboratory investigation

- Blood counts are normal early in the disease.
- Increased cholestasis parameters:**
 - » Alkaline phosphatase (ALP): ↑
 - » Gamma-GT (γ-GT): ↑
 - » Conjugated bilirubin – later stages
- LFTs: AST/ALT within normal limits or slightly raised
- Hypercholesterolemia: esp. HDL & lipoprotein X
- Increased antimitochondrial antibodies (AMA) >95%
- Increased antinuclear antibodies (ANA) - up to 70%
- Elevated serum IgM level.

Histopathological staging of primary biliary cholangitis

- ✎ **Stage-I:** Portal inflammation (lymphocytic infiltration) with granulomas
 - ✎ **Stage-II:** Bile duct proliferation, periportal inflammation (progressive fibrosis)
 - ✎ **Stage-III:** Interlobular fibrous septa (bridging fibrosis)
 - ✎ **Stage-IV:** Liver cirrhosis.
- Estimations of histologic stage by an "enhanced liver fibrosis (ELF) assay," which incorporates serum levels of hyaluronic acid, tissue inhibitor of metalloproteinase-1, and procollagen III aminopeptide, and by elastography have shown promise.

Radiological investigation

- Abdominal ultrasound:** to screen for mechanical bile obstruction
- Magnetic resonance cholangiopancreatography (MRCP):** to confirm intrahepatic bile duct occlusion
- Liver biopsy:** Performed in case of suspicion for an overlap syndrome or uncertain diagnosis (e.g., if AMA are negative but clinical suspicion is strong) and Necessary for histopathological staging of primary biliary cholangitis

Rx

- There is no cure for PBC. Treatment consists of slowing disease progression and alleviating symptoms.
 - Treatment of choice:** Liver transplantation is the only definitive treatment – necessary if liver cirrhosis is advanced
- First line:** Cap. Ursodeoxycholic acid 250mg or 500mg (Cap. Urso)
 - Dosage: 13–15 mg/kg/day in one or two divided doses (OD/BD)
 - Tab. Obeticholic acid 5mg or 10mg (Abeticolic, Ocaliva) → may be added in patients with an incomplete response or intolerance to ursodeoxycholic acid. **Initiate a dose of 5 mg OD and increased to 10 mg daily at 6 months if tolerated, based on the decline in serum ALP and bilirubin levels.** In patients with Child-Pugh class B or C cirrhosis, the recommended initial dose was 5 mg weekly; however, the drug can cause serious liver injury in patients with advanced cirrhosis, and its use in these patients has been restricted by the FDA.
 - Second line:** Cap. Fenofibrate 200mg (Fenoget, Lipofen) OR Tab. Colchicine 0.5mg x twice daily and Tab. Methotrexate 2.5mg or 10mg (Cytotrexate, Unitrexate) at dose 15mg/weekly PLUS Tab. Folic acid 5mg x OD
- For cholestatic pruritus**
- Cholestyramine 4 g sachets (Questran, Kolestean) in glass water or juice x three times daily
 - Or Tab. Rifampicin 300mg (Lederrif) at dose 150–300 mg x BD
 - Or Tab. Naltrexone 50mg x at starting dose at 12.5mg/day
 - Or Tab. Ondansetron 4mg (Onset, Onseron) x TDS
 - Or Tab. Sertraline 50mg or Tab. Sertraline 100mg (Sert) x OD
- For refractory pruritus, Plasmapheresis or extracorporeal albumin dialysis may be needed.



AMOEBIIC LIVER ABSCESS

Clinical features

- ☞ Caused by *Entamoeba histolytica*, which is spread between humans by its cysts via feco-oral route.
- ☞ Mostly acute onset of symptoms; subacute courses are rare
- ☞ **In 95% of cases:** amebic liver abscess, usually a solitary abscess in the right hepatic lobe, may not be associated diarrhoea.
 - » Patient of 20-40 years of age
 - » The commonest symptom is abdominal pain.
 - » Swinging Fever (either continuous or spiking), with chills and sweating may develops.
 - » Right upper quadrant (RUQ) pain and pressure sensation
 - » Loss of appetite (Anorexia), malaise
 - » Local discomfort, Chest pain and pleuralgia
 - » An enlarged, tender liver, cough and pain in the right shoulder are characteristic but symptoms may remain vague and signs minimal.
- ☞ **In 5% of cases:** A large abscess may penetrate the diaphragm, rupturing into the lung, and may be coughed up through a hepatobronchial fistula. Rupture into the pleural or peritoneal cavity, or rupture of a left lobe abscess in the pericardial sac, is less common but more serious. Rarely in the brain.

Diagnostic workup

- ☞ **Diagnosis is confirmed by** serological tests (ELISA) for Anti-amoebic antibodies.
- ☞ **CBC:** may show anemia, Leukocytosis, Neutrophilia
- ☞ **Liver function tests (LFTs):** Elevated level of ALP, AST, ALT, bilirubin
- ☞ **Ultrasound Abdomen:** Hypoechoic, solitary lesion in the right lobe of the liver.
- ☞ **CT scan or MRI abdomen**
 - » Well-defined, rounded lesions with contrast-enhancing wall
 - » Can be unilocular or septate
- ☞ **Ultrasound guided Aspiration of abscesses** shows chocolate-brown fluid (exudate resembles anchovy paste)



TREATMENT OF AMOEBIIC LIVER ABSCESS

1. **Tab. Metronidazole 400mg** (Flagyl, Klint, Metrozine)
2 – 2 – 2 (Dose: 750mg x TDS for 7-10 days)
OR **Tab. Metronidazole 400mg + Diloxanide Furoate 500mg** (Entamizole DS, Flagyl plus, Zolen DS) x TDS
PLUS **Tab. Metronidazole 400mg** (Flagyl, Klint)
1 – 1 – 1 (TDS)
OR **Tab. Tinidazole 500mg** (Fasygen, Prevent, Trichogin)
2 – 0 – 2 (BD) (Dose: 1g/day for 5 days)
OR **Tab. Nitazoxanide 500mg** (IZZATO, NT-TOX)
1 – 0 – 1 (Twice daily for 10 days).
 2. **With Pain/analgesia:** **Tab. Diclofenac sodium 50mg** (Voren, Voltral) OR **Tab. Mefenamic Acid 500mg** (Mefnac DS, Ponstan forte)
1 – 1 – 1 (TDS)
 3. **Gastroprotective:** **Cap. Omeprazole 40mg** (Risek, Ruling) OR **Cap. Esomeprazole 40mg** (Nexum, Esso)
0 – 0 – 1 (40mg x OD) x 30 دنے سے پہلے
- ❖ **Duration of treatment:** Clinical improvement is often seen within 72 to 96 hours, but treatment should be continued for 7 to 10 days.

Surgical drainage should generally be avoided, but may be indicated for inaccessible abscesses or ruptured abscesses in combination with peritonitis. Small serous effusions resolve without drainage.

HEMOCHROMATOSIS (IRON OVERLOAD DISEASE)

Definition: Haemochromatosis is a condition in which the amount of total body iron is increased; the excess iron is deposited in, and causes damage to, several organs, including the liver. It may be primary or secondary.

Primary (hereditary) hemochromatosis:

» **Most frequent form:** adult hemochromatosis type-I (classical form), it is Homozygous or heterozygous for the HFE gene defect, located on chromosome 6, Most commonly affects C282Y and H63D, Associated with HLA-A3 genotype. **Inheritance:** autosomal recessive with incomplete penetrance

» **Less frequent forms:** Hemochromatosis types II-IV are also hereditary

» **Secondary hemochromatosis:** caused due to iron overload

» **Transfusion-related hemochromatosis:** in patients with beta-thalassemia major or other forms of chronic anemia requiring chronic transfusion

» **Ineffective erythropoiesis:** Thalassemia, Sickle-cell anemia and Sideroblastic anemia

» **Excessive alcohol consumption**

Clinical features

» **Asymptomatic** in 75% of cases. **Age of onset** 40 years of age. Middle-aged men are more frequently and severely affected than women, Symptoms start to show when body iron levels reach >20 g. (Pre-menopause, women lose iron via menstruation and pregnancy, which slows down iron accumulation within the body. As a result, symptom onset occurs later in women (typically postmenopausal) than in men).

» **General symptoms:** Fatigue, weakness, lethargy, Increased susceptibility to infections

» **Liver features:** Abdominal pain, Hepatomegaly, Cirrhosis, Increased risk of HCC (common cause of death)

» **Pancreas involvement:** signs of diabetes mellitus (polydipsia, polyuria)

» **Skin features:** hyperpigmentation, bronze skin (Leaden-grey skin pigmentation can sometimes occur due to excess melanin, especially in exposed parts, axillae, groins and genitalia: hence the term 'bronzed diabetes').

» **Pituitary gland:** hypogonadism, impotence, testicular atrophy, loss of libido, amenorrhea

» **Joints features:** arthralgia (typically symmetrical arthropathy of the metacarpophalangeal (MCPs) joints II and III), chondrocalcinosis (accumulation of calcium pyrophosphate) and pseudogout.

» **Cardiac features:** Cardiomyopathy (due to cardiac siderosis), cardiac arrhythmias (atrial fibrillation most common, sick sinus syndrome, complete AV block, & sudden cardiac death) and Congestive heart failure.

Diagnostic workup

» **Laboratory investigation:**

» **Diagnosis of iron overload:** Elevated serum ferritin and transferrin saturation

↳ **Serum ferritin:** ↑ (> 200 ng/mL for premenopausal patients, > 300 ng/mL for all other patients. The likelihood of severe clinical complications increases with ferritin levels >1000 ng/mL).

↳ **Transferrin saturation:** ↑ (>50% in men; >45% in women), First laboratory test to become abnormal.

↳ **Serum iron:** ↑

↳ **Total iron-binding capacity (TIBC):** ↓

» **Genetic testing (HFE gene):** Confirms hereditary hemochromatosis. **Indicated** in unexplained iron overload and/or first-degree relative with hereditary hemochromatosis. **Findings:** Homozygous C282Y, homozygous H63D, or heterozygous C282Y/H63D mutation in the HFE gene confirms the diagnosis.

» **Additional investigation:**

↳ **LFTs (Hepatocellular enzymes):** ↑ AST, sometimes ↑ ALT.

↳ **CBC:** May identify iron-loading anemia (e.g., sideroblastic anemia).

↳ **Fasting blood sugar:** Elevated, should be checked in all patients with an elevated ferritin level.

» **Radiological investigation**

» **MRI liver/abdomen:** Used to estimate hepatic iron concentration (HIC). Hepatic iron pattern can help to distinguish between hereditary hemochromatosis and secondary iron overload.

» **Additional imaging:** based on symptoms

↳ **For patient with cardiac involvement:** Echo, MRI heart, &/or x-ray chest

↳ **Patient with arthritis of the 2nd & 3rd metacarpophalangeal (MCP) joints:** Plain x-ray

» **Liver biopsy:** Perl's stain quantifies iron loading (ferritin level >1000 ng/mL) & assesses disease severity, now less likely perform to assess iron overload or liver fibrosis, but often reserved for the detection of cirrhosis.

TREATMENT OF HEMOCHROMATOSIS (IRON OVERLOAD DISEASE)

Rx

Patient counselling & Lifestyle modifications:

- » In general, patients should follow a normal, healthy diet. All patients should be advised to avoid iron-fortified foods or iron-containing supplements. Vitamin C-containing supplements should also be avoided as vitamin C can lead to increased intestinal absorption of dietary iron. Despite this, some physicians may recommend low doses of vitamin C in patients who are started on parenteral iron chelation therapy. This is because it increases the availability of iron for chelation with deferoxamine.

» **Over-the-counter drugs (OTC):** Ensure vitamin preparations contain no iron. Avoid iron contain vitamins.

- » Patients should be advised to avoid excess alcohol (or avoid altogether if hepatic disease is present).
- » Raw/undercooked shellfish and wound contact with seawater should be avoided, due to susceptibility of patients with hemochromatosis to rare but serious systemic bacterial infection by *Vibrio vulnificus*.

» Hepatitis A and hepatitis B vaccinations could be considered in patients not exposed to hepatitis.

» **Early treatment of iron overload may:** Improve fatigue and skin hyperpigmentation. Reverse early organ damage (e.g., elevated liver chemistries, early cardiomyopathy). Increase life expectancy. It may be possible to prevent the progression of advanced complications, but they cannot be reversed.

» **Phlebotomy (Venesection):** indicated as first-line treatment for hereditary hemochromatosis (including asymptomatic patients). Consider in patients with secondary iron overload (e.g., for patients with symptomatic porphyria cutanea tarda)

» Contraindications

1. Inability to tolerate the procedure due to anxiety.
2. Low hemoglobin due to iron-loading anemia.
3. Conditions sensitive to fluid shifts such as end-stage liver disease, congestive heart failure.

» Therapeutic regimen:

» **Initial venesection:** 1 or 2 units (250–500mL) of blood removed weekly over 1–2 weeks; (each unit containing about 250 mg of iron), should be continued for up to 2–3 years to achieve depletion of iron stores. **Goals:** iron saturation <50% and serum ferritin of 50–100 ng/mL

» **Maintenance venesection:** 2 units (500mL) of blood removed every 2–4 months to maintain serum ferritin levels between 50–100 ng/mL, haematocrit <0.5 and transferrin saturation <40%.

» **Consider iron chelator:** it is indicated for patients with hemochromatosis and anemia or in those with secondary iron overload due to thalassemia who cannot tolerate phlebotomies.

- » **Inj. Desferrioxamine** at dose 20–40 mg/kg/day, subcutaneous (SC) or intravenous (IV) infused over 24 hours and can mobilize 30mg of iron per day; however, treatment is painful and time-consuming.
- » **Two oral chelators,** Deferasirox, 20mg/kg x OD, and Deferiprone, 25mg/kg x TDS, have been approved for treatment of iron overload due to blood transfusions and may be appropriate in patients with hemochromatosis who cannot tolerate phlebotomy.

» **Adjunct to venesection: Proton pump inhibitors (PPIs)** such as Omeprazole x at dose 40mg/day oral/IV, which reduces intestinal iron absorption, decreases the maintenance phlebotomy volume requirement.

» **Erythrocytapheresis:** Selective removal of red blood cells from the patient's circulation. Useful for patients with thrombocytopenia or hypoproteinemia.

» **Liver transplantation:** Indicated in Decompensated cirrhosis, and Hepatocellular carcinoma (HCC). **Important consideration:** Untreated iron overload is not a contraindication to transplantation. Following liver transplantation, serum iron studies and hepcidin levels are normal, and phlebotomy is not required.

» **Monitoring:** LFTs, blood glucose (Diabetes), HbA1c levels may be falsely low as venesection the time available for Hb glycosylation. If cirrhotic, screen for hepatocellular CA (HCC) with ultrasound ± AFP twice-yearly.

» **Prognosis:** Liver and cardiac problems improve after venesection (iron removal), but joint pain is less predictable and can improve or worsen after iron removal. Diabetes does not resolve. Gonadal failure may reverse in younger men. First-degree family members should be investigated, preferably by genetic screening to identify and treat other cases early. Pre-cirrhotic patients with GH have a normal life expectancy, and even cirrhotic patients have a good prognosis compared with other forms of cirrhosis (three-quarters of patients are alive 5 years after diagnosis). This is probably because liver function is often well preserved at diagnosis and improves with therapy.

WILSON'S DISEASE (HEPATOLENTICULAR DEGENERATION)

- Definition: Wilson's disease is a rare autosomal recessive disorder of copper metabolism that usually occurs in people between 3 and 55 years of age. Pathological copper accumulation leads to damage to liver, brain and other organs.
- Genetics: Autosomal recessive mutations in the ATP7B gene on chromosome 13, which encodes for a membrane-bound, copper-transporting ATPase → defective ATP7B protein.

Clinical features

- Wilson's disease (hepatolenticular degeneration) present as liver disease in adolescents (more common in females) and neuropsychiatric disease in young adults (more common in males), but there is great variability, and onset of symptoms after age 40 is more common than previously thought.
- The diagnosis should always be considered in any child or young adult with hepatitis, splenomegaly with hypersplenism, Coombs negative hemolytic anemia, portal hypertension, and neurologic or psychiatric abnormalities.
- Hepatic features:** Hepatosplenomegaly, Jaundice, Ascites, Abdominal pain, Acute or chronic hepatitis symptoms, Chronic liver disease signs (Hepatic encephalopathy, Cirrhosis, Portal hypertension, Acute liver failure symptoms)
- Ocular features:** Kayser-Fleischer rings (Golden or green-brown rings in the cornea periphery), Sunflower cataracts (Copper deposits in the lens causing sunflower-shaped opacification)
- Neurological features:** Cerebellar Symptoms (Dysarthria – most common, Gait abnormalities, Choreoathetosis), Extrapyramidal Symptoms (Dystonia, Parkinsonism, Tremor which is asymmetric, affecting hands, can be resting, intention, or wing-beating), drooling (due to oropharyngeal dysphagia), seizures, dementia and mutism
- Psychiatric and Behavioral:** Major depression, mania, Irritability, labile emotions, Psychosis
- Other features:** Haemolysis; blue lunulae (nails); arthritis; hypermobile joints; grey skin and Fanconi syndrome

Diagnostic workup

- LFTs: ↑ AST > ALT in cirrhosis ↑ Bilirubin, ↓ alkaline phosphatase in patients with ALF and/or hemolysis
- CBC: hemolytic anemia, thrombocytopenia, leukopenia may be present
- Basic metabolic panel (BNP): ↑ BUN, ↑ creatinine, ↓ potassium in renal involvement.
- Urine 24-hour copper excretion: High, e.g. >100mcg/24h (normal <40mcg).
- Serum ceruloplasmin: ↓ (< 14 mg/dL or <140 mg/L; <10 mg/dL (100 mg/L) strongly suggests the diagnosis.
- Serum copper (optional test): ↓ Total serum copper and ↑ Free serum copper (non-ceruloplasmin-bound copper)
- Molecular genetic testing can confirm the diagnosis for ATP7B mutation. Indicated in patients with either, First-degree relatives with Wilson disease or Inconclusive diagnostic tests.
- Slit lamp exam: KF rings – in iris/Descemet's membrane.
- Liver biopsy: hepatic copper (copper >250mcg/g dry weight); hepatitis; cirrhosis.
- MRI brain: degeneration in basal ganglia, frontotemporal, cerebellar, and brainstem.
- Leipzig Scoring systems may help establish the diagnosis.



TREATMENT OF WILSON'S DISEASE

- Avoid foods with high copper content such as liver, chocolate, nuts, mushrooms, legumes, soy-based products, and shellfish. Check water sources for copper (e.g. wells, pipes)
- Firstline lifelong drug: Tab. D-penicillamine 250mg (Vitamin, Penicillamine) at dose 500mg per orally 6–8 hourly (0.75–2 g/day), taken 1 hour before or 2 hours after food for 1 year, maintenance 0.75–1g/day).
- Side effects: nausea, rash, bone marrow suppression (low WCC, Hb, platelets), haematuria, nephrosis, lupus-like syndrome, if these arise, **Alternative drugs are:** Trientine dihydrochloride at dose 250–500 mg three times a day (TDS) at maximum 2000 mg/day and zinc acetate at dose 25–50mg three times daily (TDS).
- Management of hepatic symptoms** such as treatment of cirrhosis in advanced liver disease and ALF in decompensated cirrhosis. Symptomatic management of neuro and psychiatric symptoms
- Monitoring:** All patients should be regularly monitored for clinical and laboratory-based improvement and treatment of side effects. Clinical assessment, including neurological examination, at least every 6 months
- AND Laboratory tests:** At least every 6 months with serum copper, serum ceruloplasmin, liver function tests (LFTs), PT/INR, CBC, and urinalysis **AND** at least once yearly: 24-hour urine copper.
- Liver transplantation:** indicated for fulminant liver failure or for advanced cirrhosis with liver failure.
- Prognosis:** prognosis excellent with early treatment, and presymptomatic patients compliant with treatment have comparable survival to the general population. Pre-cirrhotic liver disease is reversible, CNS damage less so. There are no clear clinical prognostic indicators. Fatal events: liver failure, bleeding, infection.

ACUTE LIVER FAILURE (ALF)

Name: _____ Age: _____ Sex: _____ Date: _____
 Temperature: _____ B.P: _____ Pulse: _____ Resp. Rate: _____

☞ **Acute liver failure (ALF):** it is a rare but life-threatening condition characterized by a rapid progressive deterioration in liver function (within a period of 26 weeks) & severe acute liver injury, defined as impairment of synthetic function (i.e., coagulopathy) & encephalopathy, in an individual without previous hepatic disease.

☞ **Classification of acute liver failure**

- » **Hyper-acute liver failure:** 0 to 1 weeks (<7 days)
- » **Acute (fulminant) liver failure:** 1 weeks to 4 weeks (8 days – 28 days)
- » **Subacute liver failure:** 29 days to 12 weeks, Encephalopathy develops slowly, after = 3 weeks and up to = 26 weeks from the onset of other symptoms.
- ☞ **Acute-on-chronic liver failure (ACLF):** A distinct syndrome involving acute decompensation of chronic liver disease with features of liver failure (jaundice and coagulopathy) and other extra-hepatic organ failures. It is associated with a high short-term mortality.
- ☞ **CLD** is progressive deterioration of hepatic function over at least 26–28 weeks (=6 months) e.g. cirrhosis
- ☞ **Acute decompensation of CLD:** An episode of acute worsening of chronic liver disease manifestations (e.g., ascites, hepatic encephalopathy, gastrointestinal bleeding, jaundice, infection), which can be due to a precipitant or progression of the underlying illness.

Clinical features

Presentation is mostly non-specific, and clinicians should maintain a high index of suspicion in patients who acutely develop the following symptoms:

- ☞ **Cerebral disturbance (hepatic encephalopathy &/or cerebral edema) is the cardinal features of ALF**
 - » **Signs of hepatic encephalopathy:** Altered level of consciousness (ALOC), agitation, asterix/flap, coma
 - » **Features of cerebral edema:** headaches, vomiting, bradycardia, papilledema, ALOC, confusion, seizures
- ☞ **Gastrointestinal symptoms** (Nausea, vomiting, hematemesis, and melena)
- ☞ Systemic inflammatory response, and kidney dysfunction are common.
- ☞ Fatigue, lethargy, malaise, loss of appetite
- ☞ **Jaundice:** may be absent or minimal early in the course, but blood tests show severe hepatocellular damage.
- ☞ **Fetor hepaticus** seen in severe liver disease; smells like pear drops or musty smell on the breath & in urine.
- ☞ **Abdominal pain:** may be in the right upper quadrant (RUQ) or diffuse, secondary to ascites
- ☞ **Features of the underlying etiology:** Kayser-Fleischer rings in **wilson disease**.
- ☞ Signs of chronic liver disease suggest acute-on-chronic hepatic failure.

Diagnostic workup

- ☞ The patient should be investigated to determine the cause of the liver failure and the prognosis.
- ☞ Investigation in ALF is used to confirm the diagnosis and assess the extent of associated organ failure. When the patient is stable, investigations also aid in the identification of the underlying cause if still unknown.
- ☞ **Laboratory investigations:**
 - » **Complete blood count (CBC):** typically, platelet count $\leq 150,000/\text{mm}^3$; other findings are variable and depend on the underlying etiology.
 - » **Liver function test (LFTs):** Significantly elevated ALT & AST, $\uparrow$ Bilirubin (Hyperbilirubinemia)
 - » **Blood glucose:** $\downarrow$ (Hypoglycemia – common)
 - » **Serum electrolyte:** abnormal (e.g., hyponatremia, hypokalemia, hypophosphatemia)
 - » **BUN and creatinine:** $\uparrow$ (if acute kidney injury or hepatorenal syndrome is present)
 - » **Coagulation profile (PT, APTT & INR):** Prolonged PT and INR
 - » **ABGs:** Findings vary depending on the underlying etiology
 - ↳ **Acidosis:** secondary to lactic acidosis, uremia, or toxic metabolites
 - ↳ **Alkalosis:** secondary to hypoalbuminemic acidosis or respiratory alkalosis
 - ↳ **Lactate:** commonly elevated, marker of severe disease
 - » **Serum ammonia (preferably arterial):** frequently elevated; values > 150 micromol/L are associated with a higher risk of elevated intracranial pressure (ICP).
 - » **LDH:** typically elevated in early stages of acute liver injury

Radiological investigations: Findings vary as ALF progresses

Early findings

- » **Abdominal x-ray:** may show hepatomegaly
- » **Abdominal ultrasound:** liver echogenicity may be heterogeneously decreased (usually a sign of necrosis); possible presence of ascites
- » **Doppler ultrasound of the abdomen:** can be useful to identify the underlying cause (e.g., portal vein thrombosis, hepatic ischemia)
- » **CT scan abdomen or MRI abdomen with contrast** usually shows diffuse enhancement (e.g., in necrosis), may show ascites and/or hepatomegaly

Findings in late stages: In patients who have been sick for at least seven days, Ultrasound, CT scan, or MRI may show a nodular surface, which can be mistaken for cirrhosis.

Test to identify the underlying cause: The etiology of ALF may be evident after taking the patient history (for example paracetamol overdose), or it may require further investigation. In many cases, the etiology remains unknown even after an extensive evaluation.

Laboratory test

- » **Screen the following viral serologies in all patients:** Hepatitis-A (IgM), hepatitis-B (surface antigen and core IgM), hepatitis C (antibodies), and hepatitis E (IgG and possibly RNA testing)
 - Consider PCR for EBV, CMV, adenovirus, and HSV.
 - Consider VZV (IgM) in immunocompromised patients or those with a vesicular rash.
- » **Toxicology screen:** measure paracetamol levels and consider screening for other measurable hepatotoxic drugs, e.g., phenytoin.
- » **Consider testing for more uncommon etiologies based on clinical suspicion:** Ceruloplasmin and copper level for wilson disease, Serum IgG levels & autoimmune markers for autoimmune hepatitis, alpha-fetoprotein for suspected malignancy and Pregnancy test in suspected HELLP syndrome
- » **Hematologic test:** Peripheral blood smear and coomb's test may show abnormalities, e.g., hemolytic anemia in wilson disease.
- » **Microbiology** Blood culture; urine culture; ascitic tap for MC&S of ascites → neutrophils >250/mm³ indicates spontaneous bacterial peritonitis

Liver biopsy → Indication: To distinguish between acute liver failure (ALF) and chronic liver disease (CLD), if the diagnosis is uncertain. The suspected underlying etiology requires specific management for example autoimmune hepatitis, malignancy.

King's College Hospital criteria in acute liver failure

Paracetamol-induced liver failure	Non-paracetamol liver failure
Arterial pH <7.3 24h after ingestion.	PT >100s
Or all of the following:	Or 3 out of 5 of the following:
Prothrombin time (PT) >100s	1. Drug-induced liver failure
Creatinine >300μmol/L.	2. Age <10 or >40yrs old
Grade III or IV encephalopathy	3. > 1 week from 1st jaundice to encephalopathy.
	4. PT >50s
	5. Bilirubin ≥300μmol/L.

Fulfilling these criteria predicts a poor outcome in acute liver failure and should prompt consideration for transplantation. Based on O'Grady J et al. 'Early indicators of prognosis in fulminant hepatic failure.' Gastroenterology, 97(2):439-45, 1989.



TREATMENT OF ACUTE LIVER FAILURE (ALF)

- » **Beware of sepsis, hypoglycaemia, GI bleeds/esophageal varices, and encephalopathy**
- » **Admit the patient in high-dependency unit (HDU) or intensive care unit (ICU)**
- » **Stabilize patients using ABCD&E approach.**
 - » Protect the airway with intubation
 - » Check spO₂ and Provide Oxygen supplementation, aims to keep saturation 94-98.
 - » Head-end of the bed to 30° to reduce raised ICP/cerebral edema.
 - » Insert an NG tube to avoid aspiration and remove any blood from stomach.
 - » Insert urinary and central venous catheters to help assess fluid status.

- ☛ Establish large-bore intravenous (IV) access.
- ☛ Vitals monitoring: Check BP, Pulse, RR, Temperature, SpO₂, pupils, urine output hourly and daily weights.
- ☛ Obtained labs: Check CBC, BUN, Electrolytes, LFTs, and PT/INR daily and septic workup if indicated.
- ☛ IV fluids therapy: Give 10% Dextrose x 1L x 12 hours to avoid hypoglycaemia with a target glucose ~140 mg/dL. Do blood glucose every 1–4h. Avoid hypotonic fluids (may result in hyponatremia).
- ☛ Optimize nutrition: for patients in a catabolic state/malnourished, optimize weight-based protein (1–1.5 g/kg/day) intake enterally or via TPN with careful monitoring of the ammonia level. To preserve muscle mass and immune function, good nutrition can decrease mortality. Give thiamine and folate supplement.
- ☛ Treatment of seizures (see emergency chapter – treatment of status epilepticus)
- ☛ Treatment of renal injury/failure: Haemofiltration or haemodialysis, if renal failure develops
- ☛ Avoid precipitating drugs: Try to avoid sedatives and other drugs with hepatic metabolism. Avoid drugs that constipate (risk of encephalopathy), oral hypoglycemics, and saline-containing IVIS. Warfarin effects are enhanced. Hepatotoxic drugs include such as Paracetamol, methotrexate, isoniazid, azathioprine, phenothiazines, oestrogen, 6-mercaptopurine, salicylates, tetracycline, mitomycin.
- ☛ Gastroprotective to prevent stress ulceration: Omeprazole 40mg (Ruling, Omezol) x IV/PO.

☛ Management of complications

- » Cerebral edema: Consider CT brain. 20% mannitol IV; hyperventilate, head of bed elevation at 30°.
- » Ascites: Restrict fluid, low-salt diet, weigh daily, give diuretics (furosemide, spironolactone)
- » GI Bleeding: Inj. Vitamin K 10mg/day IV for 3 days, platelets, FFP + blood as needed ± endoscopy.
- » Blind of infection: Inj. Ceftriaxone 1–2g (Oxidil) x once daily (OD) x IV, not gentamicin (risk of renal failure).
- » Hypoglycemia: treatment of hypoglycemia as needed with 50mL of 50% dextrose IV; check often.
- » Encephalopathy: Avoid sedatives; correct electrolytes; **Syp. Lactulose** (Duphalac, Lilac) at 30–50mL every 8 hour (aim for 2–4 soft stools/day) is catabolized by bacterial flora to short chain fatty acids which colonic pH and trap NH₃ in the colon as NH₄⁺; **Tab. Rifaximin 550mg** (Rifixa) every 12h is a non-absorbable oral antibiotic that numbers of nitrogen-forming gut bacteria.
- » Sepsis: Screen for sepsis and start empiric antibiotics for sepsis if suspected. (see treatment of sepsis)

☛ Identify and treat the underlying cause, if known:

- » **Paracetamol toxicity:** Start treatment with N-acetylcysteine (NAC).
 - ☛ **IV N-acetylcysteine (NAC)** at dose 150mg/kg in 5% dextrose x IV infusion loading dose given over 1 hr, then 50mg/kg IV infusion over 4 hrs, followed by 100mg/kg IV infusion over 16 hrs (total 300 mg/kg)
 - ☛ **OR Oral N-acetylcysteine** at dose 140mg/kg orally followed by 70mg/kg orally every 4 hours for an additional 17 doses, prevents paracetamol toxicity if administered within 12 hours of ingestion and may be beneficial when given up to 72 hours after ingestion.
- » **Autoimmune hepatitis:** Consider a trial of steroids on a case-by-case basis, weighing the increased risk of infection against the likely benefit. Firstline is prednisolone with or without azathioprine (AZA)
- » **Viral hepatitis:** supportive & antiviral treatment, depending on the cause (HBV infection, HSV hepatitis)
- » **Phalloides poisoning (Mushroom poisoning):** Start treatment with silibinin (silymarin or milk thistle) or Penicillin G (300,000 to 1 MU/kg/day), consider N-acetylcysteine (NAC).
- » **Pregnancy-associated liver diseases:** Urgent delivery of the fetus is indicated.
- » **Wilson disease:** Plasmapheresis combined with D-penicillamine

- ☛ **Liver transplant:** Consider liver transplant in most patients, as a high proportion do not recover with supportive therapy alone. Using scoring system as King's College criteria. For patients who require transplant → Refer immediately to a transplant center, obtain a pretransplant evaluation and infectious workup.

- ☛ **Prognosis:** worse prognosis if Grade III–IV encephalopathy, age > 40 years, albumin <30g/L, INR, drug-induced liver failure, late-onset hepatic failure worse than fulminant failure. Survival following liver transplantation for acute liver failure is improving and 1-year survival rates of 80%–90% can be expected.



DIABETES MELLITUS

DIAGNOSTIC APPROACH

- History is extremely important to determine whether a patient has new-onset hyperglycemia as opposed to untreated or poorly controlled pre-existing diabetes mellitus.
- » Distinguishing between type 1 diabetes mellitus and type 2 diabetes mellitus, along with new-onset hyperglycemia, can help establish a clear plan for glycemic control during hospital admission.
 - » For example, a higher vigilance for diabetic ketoacidosis is important in patients with type 1 diabetes.
- Examination: Patients should undergo a complete physical exam specific to their presenting condition
- » **Eye exam:** Fundus exam with an ophthalmoscope to assess for diabetic retinopathy.
 - » **Vibration sense and microfilament exam:** a screening exam, using simple tests such as pinprick sensation, vibration perception (using a 128-Hz tuning fork), 10-g monofilament pressure sensation, and assessment of ankle reflexes to assess for signs of diabetic neuropathy.
- Diagnostic test:
1. **Fasting blood glucose (FBS) level:** ≥ 126 mg/dl (≥ 7.0 mmol/L).
 2. **Random blood glucose (RBS) level:** ≥ 200 mg/dl (≥ 11.1 mmol/L).
 3. **75g Oral glucose tolerance test (OGTT) – Diagnostic test**
 - » Plasma glucose is measured 2 hours after 75g oral glucose load. Patient should be advised to consume a varied diet with at least 150 g of carbohydrate on the 3 days prior to testing, as fasting and carbohydrate restriction can falsely increase plasma glucose levels.
 - » **Normal value:** < 140 mg/dL (< 7.8 mmol/L) in healthy person
 - » **Impaired glucose tolerance:** 140–199 mg/dL (7.8–11.0 mmol/L)
 - » **Capillary blood sugar level should not be used in the diagnosis of DM**
 - » **Venous blood sugar level should be used in the diagnosis of DM.**
 4. **Glycosylated hemoglobin-A1c (HbA1c) test:** HbA1c indicates glucose levels from the previous 8-12 weeks. Half-life of RBC is 2-3 months that's why HbA1c should be monitor every 3-4 months.
Interpretation of HbA1c: **Normal value:** $< 5.7\%$ in a healthy person. **Prediabetes:** 5.7% – 6.4%, Patients are at an increased risk of developing DM (Insulin resistance) and **Diabetes mellitus:** $\geq 6.5\%$
 5. **BUN, serum creatinine and GFR calculation:** may be abnormal in diabetic nephropathy/renal insufficiency
 6. **Spot urine for albumin/creatinine ratio (ACR):** Microalbuminuria (an early sign of diabetic nephropathy)
 - » < 30 micrograms/mg creatinine is normal and excludes diabetic nephropathy.
 - » Microalbuminuria has historically been defined as 30-299 micrograms/mg creatinine.
 - » Macroalbuminuria has historically been defined as ≥ 300 micrograms/mg creatinine.
 7. **Additional test if indicated:**
 - » **Urinalysis:** Urine ketone bodies (usually accompanied by glucosuria) **+Ve** in DKA & microalbuminuria
 - » **Specific auto-antibodies for diabetes mellitus type-1:** Anti-GAD antibodies, Anti-tyrosine phosphatase-related islet antigen (IA-2), Islet cell surface antibody (ICSA; against ganglioside)
 - » **Random C-peptide level:** Decrease (< 0.2 nmol/L) or undetectable levels indicate an absolute insulin deficiency $\rightarrow$ T1DM & increase level (> 1 nmol/L) indicate insulin resistance & hyperinsulinemia $\rightarrow$ T2DM
 - » **Fasting lipid profile:** may show high LDL, low HDL, and/or high triglycerides
 - » **Liver function tests (LFTs):** Liver enzymes may be deranged in T2DM and fatty liver disease
 - » **ECG:** may indicate prior ischemia

DIAGNOSTIC CRITERIA FOR THE DIAGNOSIS OF DIABETES MELLITUS

Criteria for the diagnosis of diabetes (American Diabetes Association)

- » Sign and symptoms of DM/Hyperglycemia + Fasting blood sugar (FBS) ≥ 126 mg/dl (≥ 7.0 mmol/L).
- » OR Sign and symptoms of DM/Hyperglycemia + Random blood sugar (RBS) ≥ 200 mg/dl (≥ 11.1 mmol/L).
- » OR FBS ≥ 126 mg/dl or RBS ≥ 200 mg/dl in 2 separate time/occasion
- » OR FBS ≥ 126 mg/dl + 75g Oral glucose tolerance test (OGTT) 2 hour ≥ 200 mg/dL (≥ 11.1 mmol/L).
- » OR HbA1c $\geq 6.5\%$ (≥ 48 mmol/mol) on two separate occasions, or a single HbA1c $\geq 6.5\%$ (≥ 48 mmol/mol) in combination with either a fasting glucose ≥ 126 mg/dL (≥ 7.0 mmol/L) or a random plasma glucose of ≥ 200 mg/dL (≥ 11.1 mmol/L), is diagnostic of diabetes.



DIABETES MELLITUS TYPE-1 (T1DM)

CLINICAL FEATURES

- » **Onset:** often sudden, diabetic ketoacidosis (DKA) is the first manifestation in approximately one-third of cases.
- » **Classic symptoms of hyperglycemia:** Polyuria, Polydipsia, Polyphagia
- » **Nonspecific symptoms:** Thin appearance, young age, unexplained weight loss, visual disturbances (blurred vision), fatigue, pruritus, calf cramps, poor wound healing, increased susceptibility to infections (e.g. UTI, Candidal infections) and DKA (these patient have symptoms of dehydration and acidosis such as nausea, vomiting, abdominal pain, tachypnea, tachycardia, lethargy, and altered mental status)

GENERAL PRINCIPLES OF MANAGEMENT

- » **Main goal:** Blood glucose control, tailored to glycemic targets and regularly monitored
- » **Comprehensive diabetes care (all patients)**
 - » **Continuous patient education**
 - » **Lifestyle Modification**
 - » Weight reduction, smoking cessation and alcohol reduction (no more than 14 units/week for an adult)
 - » **Balanced diet and nutrition:** Avoidance of sugars, concentrated sweets and foods high in saturated fats and cholesterol, advice a high-fiber diet & eating nonstarchy vegetables, whole foods & grains
 - » **Regular exercise:** American Diabetes Association (ADA) recommends that all adults with diabetes reduce sedentary time (avoiding periods > 90 minutes) and do either 150 minutes/week of moderate-intensity exercise (such as brisk walking, biking, or swimming) or 75 minutes/week of vigorous-intensity exercise. Muscle-strengthening exercises (e.g. yoga, Tai-chi) 2-3 times/week.
 - » **Consider low calorie sweetener:** Tab. Canderel, Tab. Clio, Tab. Hermesetas
 - » **Consider vitamin-B complex supplementation:** Tab. Neurobion, Tab. Bevidox x once daily
- » **Monitor patient's glycemic control annually:** HbA1c of <6.5% (<48mmol/mol) is ideal.
- » **Starting dose calculation in type-1 DM**
 - » Exogenous insulin requirements will depend on the residual insulin production of the pancreas.
 - » **Total daily dose (TDD) of insulin:** usually 0.4 – 1.0 units/kg/day, divided into 50% basal and 50% prandial insulin based on weight of the patient.
 - » **Consider starting insulin treatment with dose:** 0.5 units/kg/day.
- » **Dose titration**
 - » After beginning insulin treatment, there is often a temporary reduction in exogenous insulin demand.
 - » Insulin can be given 15-30 minutes before every meal
 - » Dosage should be titrated and adjust according to blood sugar level (glycemic monitoring)

DESIGNING A REGIMEN

- » Basal insulin can be administered as a basal rate of RAPID-ACTING INSULIN via an insulin pump, or as daily injections of a long-acting insulin. Patients on an insulin pump will take prandial insulin as a bolus before each meal.
- » For those on MDI, the simplest approach to covering mealtime insulin requirements is to suggest a range of doses, such as 4 units for a small meal, 6 units for a medium-sized meal, and 8 units for a larger meal. However, for greater flexibility of carbohydrate content of meals, pre-meal insulin should be calculated based on the estimated amount of carbohydrate in the meal and the patient's individual insulin-to-carbohydrate ratio. A simple beginning approach is to use 1 unit of mealtime insulin for every 15 g of carbohydrate in the meal.
- » A correction dose may be added to the bolus insulin based on the pre-meal blood glucose level. Correction dosing may be calculated as follows when the patient's total daily dose of insulin (TDD) and food intake is stable: $1800/TDD = \text{the predicted point drop in blood glucose per unit of rapid-acting insulin}$. For example, if the TDD is 40 units of insulin, $1800/40 = 45$ -point drop per unit of insulin.

Rx

TREATMENT OF TYPE-1 DIABETES MELLITUS

- » **MDI/Basal-bolus insulin regimens:** refer using a combination of rapidly acting insulin analogs and long-acting insulin analogs allows for more physiologic insulin replacement.
 - » **Rapidly acting insulin analogs:** insulin regular, insulin lispro, or insulin aspart, or insulin glulisine
 - » **PLUS, Long-acting insulin analogs:** insulin glargine, insulin detemir, or insulin degludec
 - » **OR Alternative – intermediate-acting insulin:** insulin NPH or isophane
- » **OR Insulin pump:** The insulin pump uses rapid-acting insulin and provides a basal rate of insulin and delivers mealtime bolus dosing. When used with an integrated CGM system, the pump can adjust the insulin delivery rates to maintain glucose levels in a pre-set target range.

Multiple daily injections (MDI) insulin regimens

Insulin analogs	Pre-breakfast	Pre-lunch	Pre-dinner	At bedtime
Rapidly acting insulin analogs (any listed below)	5 units	4 units	6 units	
Long-acting insulin analogs: insulin detemir x BD	6–7 units			8–9 units
OR				
Rapidly acting insulin analogs (any listed below)	5 units	4 units	6 units	
Long-acting insulin analogs: Insulin glargine or insulin degludec x only once a day				15–16 units



TREATMENT OF TYPE-1 DIABETES

1. Rapidly acting insulin injection:

- ✎ Insulin regular (Insuget R, Humulin-R, Actrapid)
OR Insulin lispro (Humalog, Humalog kwikPen)
OR Insulin aspart (NovoRapid Flexpen, NovoMix30)
OR Insulin glulisine (Apidra, Apidra SoloStar)
- ✎ 4–6 units three time daily (pre-breakfast, pre-lunch and pre-dinner), dosage should be titrated and adjust according to blood sugar level of the patient.

2. OR Long-acting insulin injection:

- ✎ Insulin detemir (Levemir, Levemir Flexpen) x 6–7 units pre-breakfast and 8–9 units at bedtime x Twice daily
OR Insulin glargine (Lantus, Basagline, Lantus SoloStar, Toujeo SoloStar) x at dose 15–16 units x once daily at the same time each day, preferably at night.
OR Insulin degludec (Tresiba Flexpen) x at dose 15–16 units x once daily at the same time each day in the morning or evening or any other time of the day.
OR Insulin NPH (Insuget-N, Humulin-N) x Twice daily (BD)



Treatment with Premix insulin (prescription #2)

- ✎ Regular insulin injection (Insuget R, Humulin-R, Actrapid)
100 units/ml subcutaneous use (SC) x BD
✎ 8–12 units before breakfast (Morning), 8–12 units before lunch & 6–8 units before dinner (Evening)
- ✎ if not controlled than add:
- ✎ 70% human insulin isophane & 30% human insulin rDNA origin (Humulin 70/30, Insuget 70/30)
✎ 4–6 units before dinner (Evening)

Patients should follow up for

- 1) Diabetic ketoacidosis
- 2) Hypoglycemia
- 3) Eye: Diabetic cataract, Diabetic retinopathy, Glaucoma
- 4) Diabetic kidney disease/ Diabetic nephropathy
- 5) Diabetic neuropathy (autonomic and peripheral neuropathy)
- 6) Cardiovascular disease (CVS): heart disease (MI), Hypertension and peripheral vascular diseases.

7) Lipoatrophy (Observe Injection sites)

8) Diabetic foot

9) **Dermatological:** Type 1 diabetes may be associated with autoimmune skin diseases such as necrobiosis lipoidica, granuloma annulare, vitiligo, and bullosis diabeticorum. In addition, there is a small risk of insulin-induced lipodystrophy, allergic contact dermatitis caused by insulin pumps or CGM sensors or adhesives, and infection at site of insertion

10) Depression and eating disorder

MDI INSULIN REGIMENS

- ✎ Using a combination of long-acting insulin (insulin glargine, insulin detemir, or insulin degludec) or intermediate-acting insulin (insulin NPH [Neutral Protamine Hagedorn]/isophane) for basal dosing, and rapid-acting insulin (insulin lispro, insulin aspart, or insulin glulisine) or short-acting insulin (regular/human insulin) for bolus dosing, MDI regimens can be designed based on physician and patient preference and modified based on finger-stick data.
- ✎ Treatment with analog insulins may provide the benefit of increased flexibility of lifestyle and less hypoglycemia as compared with human insulins. In fact, in patients who are at high risk of hypoglycemia, the Endocrine Society recommends using long-acting insulin analogs rather than insulin NPH for those on basal insulin therapy, and rapid-acting insulin analogs rather than short-acting human insulins for those on basal-bolus insulin. However, insulin analogs are more expensive. Biosimilars of analog insulin may be available in some countries at a lower cost, making them more affordable. Ultra-rapid acting insulin analogs are also available for a more favorable postprandial glycemic effect.

INSULIN – ANTIDIABETICS/ANTI-HYPERGLYCEMIC DRUGS

ULTRA SHORT (RAPIDLY) ACTING HUMAN INSULIN ANALOGS	
Insulin lispro	Inj. Humalog 100 units/ml x SC Inj. Humalog kwikPen 100 units/ml x SC
Insulin aspart	Inj. NovoRapid Flexpen 100 units/ml x SC Inj. NovoMix30 100 units/ml x SC
Insulin glulisine	Inj. Apidra 100 units/ml x SC Inj. Apidra SoloStar 100 units/ml x SC
SHORT-ACTING REGULAR INSULIN	
Insulin regular (Human insulin – rDNA origin)	Inj. Humulin-R 100 units/ml x SC/IV Inj. Insuget-R 100 units/ml x SC/IV Inj. Actrapid 100 units/ml x SC/IV
INTERMEDIATE-ACTING INSULINS	
Human insulin (rDNA origin) & human insulin isophane NPH = (Neutral protamine Hagedorn) – AKA Isophane	Inj. Humulin-N (NPH) 100 units/ml x SC Inj. Insuget-N 100 units/ml x SC
PRE-MIXED INSULINS	
Insulin lispro (25%) & insulin protamine (75%)	Inj. Humalog Mix25 100 units/ml x SC Inj. Humalog Mix25 kwikPen 100 units/ml x SC
Insulin lispro (50%) & insulin protamine (50%)	Inj. Humalog Mix50 100 units/ml x SC Inj. Humalog Mix50 kwikPen 100 units/ml x SC
Insulin aspart (30%) & insulin aspart protamine (70%)	Inj. Novolog 30/70% FlexPen x 100 units/ml x SC Inj. Novomix 30/70% FlexPen x 100 units/ml x SC
Human insulin isophane (70%) & human insulin (30%)	Inj. Humulin 70/30 100 units/ml x SC Inj. Insuget 70/30 100 units/ml x SC
Insulin degludec (70%) & insulin aspart (30%)	Inj. Ryzodeg Flexpen 100 units/ml x SC
LONG-ACTING HUMAN INSULIN ANALOGS	
Insulin glargine	Inj. Lantus 100 units/ml x SC Inj. Basagine 100 units/ml x SC Inj. Lantus SoloStar 100 units/ml x SC Inj. Toujeo SoloStar 300 units/ml x SC
Insulin detemir	Inj. Levemir 100 units/ml x SC Inj. Levemir Flexpen 100 units/ml x SC
Insulin degludec	Inj. Tresiba Flexpen 100 units/ml x SC
LONG-ACTING INSULIN + GLP-1 RECEPTOR BLOCKER	
Insulin degludec + Liraglutide	Inj. Xultophy 100/3.6 100 units/ml x SC

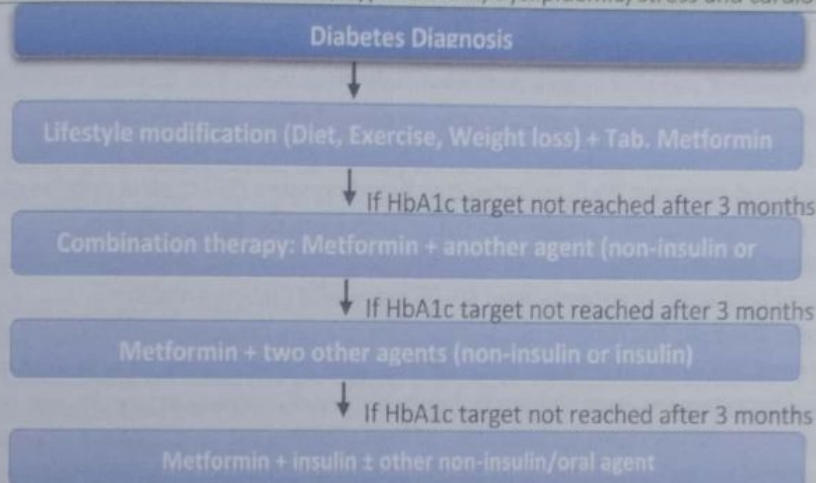
CHARACTERISTICS OF INSULIN THERAPY

TYPES OF INSULIN	ONSET OF ACTION	PEAK ACTION	EFFECTIVE ACTION	FREQUENCY OF INSULIN INTAKE	CONTROLLING SUGAR LEVEL TYPE
Ultra-short acting insulin ☞ Lispro insulin ☞ Aspart insulin ☞ Glulisine insulin	5 to 15 minutes	1 to 1.5 hour	2 to 4 hours	TID with meal	Control sugar level after each meal (insulin should be given before 15-30 minutes)
Short-acting insulin ☞ Regular Insulin				TID with meal	
Intermediate acting insulin ☞ NPH insulin (Neutral protamine Hagedorn)	30 to 60 minutes	2 hours	6 to 8 hours	Two times a day (BID)	After lunch sugar and after dinner to control Fasting blood sugar
Long-acting insulin ☞ Glargine insulin ☞ Detemir insulin ☞ Degludec insulin	2 to 4 hours	6 to 7 hours	10 to 20 hours	Once a day at same time, preferred at bedtime	Control all day sugar level
	0.5 to 1 hour	Flat	≈24 hours		
	0.5 to 1 hour		17 hours		
	0.5 to 1.5 hour		>42 hours		

DIABETES MELLITUS TYPE-2 (T2DM)

Clinical features

- Onset: typically, gradual. Most patients are asymptomatic. Some patients may present with a hyperglycemic crisis. Elderly patients especially may present in a hyperosmolar hyperglycemic state, occasionally, patients with T2DM present with DKA, which mostly affects black and Hispanic individuals.
- Symptoms of complications may be the first clinical sign of disease.
- Classic symptoms of hyperglycemia: Polyuria, Polydipsia, Polyphagia
- Nonspecific symptoms: Unexplained weight loss, blurred vision, fatigue, pruritus, poor wound healing, increased susceptibility to infections (UTI, Skin infections, Candidal infections), calf cramps and paresthesias
- Possible cutaneous signs of insulin resistance: Benign Acanthosis nigricans, Acrochordons (Benign Skin tags)
- Risk factors: older age (> 30), obesity (overweight), physical inactivity, family history of first degree relative with T2DM, gestational diabetes, pre-diabetes, PCOS, hypertension, dyslipidemia, stress and cardiovascular diseases



DIABETES MELLITUS TYPE-2 TREATMENT ALGORITHM

ASCVD = Atherosclerotic Cardiovascular Disease; CVD = Cardiovascular Disease; DPP-4 = Dipeptidyl Peptidase 4; DPP-4-i = DPP-4 inhibitor; GLP-1 = glucagon-like peptide 1; HBA1C = glycosylated hemoglobin; SGLT-2 = sodium-glucose cotransporter-2; SU = sulfonylurea; TZD = thiazolidinedione.

NON-INSULIN ANTIDIABETICS FOR THE TREATMENT OF T2DM

Drug class	Drug Brand	Important considerations
Biguanides: Metformin	Tab. Glucophage	Drug of choice, unless there are contradictions for metformin. Causes weight loss, lactic acidosis
Strength: 250, 500, 850mg, 1000mg	Tab. Neophage	
Dipeptidyl peptidase-4 inhibitor (DPP4 inhibitors): Sitagliptin	Tab. Sitagen	Well tolerated, weight-neutral, do not cause hypoglycemia. Causes: Nasopharyngitis, URTI Avoid saxagliptin in patients with heart failure
Strength: 50mg, 100mg	Tab. Trevia	
SGLT-2 inhibitors:	Tab. Emglip	Consider in patients with clinical ASCVD or high risk of ASCVD, CKD, or CHF.
Empagliflozin: 10mg, 25mg	Tab. Emptor	
Dapagliflozin: 5mg, 10mg	Tab. Dapa	Beneficial for obese or patients who need to weight loss or maintain their weight.
	Tab. Xiga	
GLP-1 receptor agonists		Consider in patients with clinical ASCVD, high risk of ASCVD, or CKD.
Semaglutide: 3mg, 7mg, 14mg	Tab. Reybelsus x orally	
Semaglutide: 0.25mg, 0.5mg, 1mg	Inj. Ozempic x SC	Beneficial for obese or patients who need to weight loss or maintain their weight. Semaglutide and liraglutide have been showing kidney protective effects
Liraglutide: 6mg/ml x once daily, SC	Inj. Victoza, Inj. Saxenda	
Dulaglutide: 0.25mg/0.5ml, 0.5mg/0.5ml, 1.5mg/0.5ml x weekly	Inj. Trulicity x SC	Increases risk for hypoglycemia, weight gain May reduces microvascular complication
Sulfonylureas (SU): Glimepiride	Tab. Amaryl	
Strength: 1mg, 2mg, 3mg & 4mg	Tab. Getryl	Causes: weight gain, edema (fluid retention), anemia, bone fracture, avoid in CHF patients. Pio-Potential ↑ MI, Rosi- bladder cancer
Thiazolidinedione (TZD)		
Pioglitazone: 15mg, 30mg	Tab. Piozer	
Rosiglitazone: 2mg, 4mg & 8mg	Tab. Rosita	

For combination drug therapy see BELOW Hypoglycemic agent in Pakistan

GENERAL PRINCIPLES FOR T2DM

- ☞ **Main goal:** Blood glucose control, tailored to glycemic targets, regularly monitoring and treatment of comorbidities
- ☞ **Comprehensive diabetes care (all patients)**
 - » **Continuous patient education (self-management training):** Since diabetes is a lifelong disorder, education of the patient and the family is probably the most important obligation of the clinician who provides care.
 - » **Life-style modification**
 - ☞ **Weight reduction, smoking cessation and alcohol reduction** (no more than 14 units/week for an adult)
 - ☞ **Well Balanced, nutrition diet:** Avoidance of sugars, concentrated sweets and foods high in saturated fats and cholesterol, advice a high-fiber diet and eating nonstarchy vegetables, whole foods and grains
 - ☞ **Regular exercise:** American Diabetes Association (ADA) recommends that all adults with diabetes reduce sedentary time (avoiding periods >90 minutes) and do either 150 minutes/week of moderate-intensity exercise (such as brisk walking, biking, or swimming) or 75 minutes/week of vigorous-intensity exercise. Muscle-strengthening exercises (e.g. yoga, Tai-chi) 2-3 times/week.
 - ☞ **Consider low calorie sweetener:** Tab. Canderel, Tab. Clio, Tab. Hermesetas
 - ☞ **Consider vitamin-B complex supplementation:** Tab. Neurobion, Tab. Bevidox x once daily
- » **Routine screening for and management of common comorbidities and complications**
- » **Atherosclerotic Cardiovascular Disease (ASCVD) risk assessment, prevention and management:**
 - ☞ **Control of blood pressure:** Well, accepted that blood pressure (BP) control reduces cardiovascular risk in patients with diabetes → consider anti-hypertensive see cardiology section
 - ☞ **Control blood lipids:** Initiate moderate-intensity statin therapy (e.g. Atorvastatin, Rosuvastatin), regardless of lipid levels in patients aged 40–75 years with diabetes mellitus
 - ☞ **Anti-platelet therapy:** The routine use of aspirin for primary prevention of diabetic CVD is not generally recommended. However, in patients with diabetes ages ≥50 years who have at least one additional risk factor (e.g., hypertension, hyperlipidemia, family history of coronary artery disease, current or past smoker, or CKD) and who have no indicators of high bleeding risk (e.g., anemia or prior significant bleeding episodes), aspirin therapy may be considered as a primary prevention strategy following discussion on the benefits versus increased risk of bleeding.

TREATMENT GUIDELINES FOR T2DM

1. **Start treatment in all patients at diagnosis.**
 - » Monotherapy (single drug therapy) with metformin is the first-line initial treatment for most patients.
 - » If there are contraindications to metformin, we choose an alternative glucose-lowering medication guided by patient comorbidities, preferences, and cost.
 - ☞ **Existing cardiovascular and/or kidney comorbidities** – For patients with cardiorenal comorbidities who cannot take metformin, we suggest a GLP-1 receptor agonist (liraglutide, semaglutide, or dulaglutide) or a SGLT2 inhibitor (Empagliflozin, Canagliflozin, or Dapagliflozin).
 - ☞ **In the absence of ASCVD, heart failure (HF), or Diabetic kidney disease (DKD):**
 - **For patients without cardiorenal disease, and with HbA1C levels relatively far from goal** (e.g., >9% [74.9 mmol/mol], without suspected T1DM), we suggest insulin or a GLP-1 agonist for initial therapy.
 - **For similar patients but with HbA1C levels ≤9%**, options (in addition to insulin or GLP-1 receptor agonists) include sulfonylureas, SGLT2 inhibitors, dipeptidyl peptidase (DPP-4) inhibitors, Repaglinide or pioglitazone. Each one of these choices has individual advantages and risks. Choice of medication is guided by efficacy, patient comorbidities, preferences, and cost. Sulfonylureas remain a highly effective treatment for hyperglycemia, particularly when cost is a barrier. Side effects of hypoglycemia and weight gain can be mitigated with careful dosing and diabetes self-management education.
2. **Consider initial or early dual therapy with a noninsulin antidiabetic in certain patients, e.g., those with:**
 - Clinical ASCVD or high ASCVD risk
 - HbA1c ≥1.5 – 2.0% above the glycemic target
3. **Consider the necessity for early combination therapy with insulin.**
4. **Reevaluate treatment and treatment adherence every 3–6 months.**
 - Sequentially add non-insulin antidiabetic drugs until glucose targets are met.
 - **If targets are still not met despite adequate treatment:**
 - Add an injectable Glucagon-like peptide-1 (GLP-1) receptor agonist
 - Consider insulin therapy.

INDICATIONS FOR INSULIN THERAPY IN T2DM

- Patients whose glycemic targets are not met despite sufficient antidiabetic treatment
- Patients with contraindications for non-insulin antidiabetic drugs, e.g., patients with end-stage renal failure
- Pregestational and gestational diabetes
- Hyperglycemic crisis
- Consider in newly diagnosed patients with any of the following:
 - Initial glucose ≥ 300 mg/dL (≥ 16.7 mmol/L) or HbA1c $> 10\%$ (> 85.8 mmol/mol)
 - Symptoms of hyperglycemia (e.g., with polyuria, polydipsia, or unintentional weight loss)
 - Signs of a continued catabolic state, e.g., Ketonuria and/or weight loss

APPROACH TO INSULIN TREATMENT IN T2DM

- Start with the simplest insulin regime, i.e., a Basal insulin regimen with once-daily injections.
- Titrate the insulin dose according to individualized glycemic targets and tolerance.
- Consider adding prandial insulin or switching to a mixed insulin regimen as needed.

TREATMENT OF TYPE 2 DIABETES MELLITUS (T2DM)

Atherosclerotic Cardiovascular Disease (ASCVD) risk prevention, & management in patient with T2DM

- Blood pressure control management (see cardiology section – hypertension):
 - Tab. Lisinopril 5mg OR 10mg (Zestril) at dose 5mg x orally once daily initially, increase gradually to 10mg according to response. **Maximum:** 40 mg/day.
 - OR Tab. Losartan 25mg OR 50mg (Eziday, Sartan) at dose 25 mg orally once daily initially, increase gradually 50mg according to response. **Maximum:** 100 mg/day.
- Lipid control management → initiate moderate intensity statins
 - Tab. Atorvastatin 10mg OR 20mg (Statin, Lipitor) at dose 10-20 mg x orally x once daily
 - OR Tab. Rosuvastatin 5mg OR 10mg (Crestor, X-Plended) at dose 5-10 mg x orally once daily
- Anti-platelets therapy for secondary prevention:
 - Tab. Aspirin 75mg (Loprin, Ascard) start at dose 75mg (up to 150mg) x per orally, once daily
 - OR if contraindication/intolerance to aspirin: Tab. Clopidogrel 75mg (Lowplat, Plavix) x orally once daily
 - OR for patients with stable coronary &/or peripheral artery disease: Tab. Aspirin 75mg OR 150mg (Loprin, Ascard) at dose 75-150 mg once daily AND Tab. Rivaroxaban 2.5mg (Revoban, Xcept, Rivaxo) x twice daily
 - OR Dual antiplatelet therapy for patients with Acute coronary syndrome: Aspirin + Ticagrelor OR Clopidogrel
 - Tab. Aspirin 75mg OR 150mg (Loprin, Ascard) at dose 300 mg orally as a loading dose, followed by 75-150mg once daily AND Tab. Ticagrelor 90mg (Anplag, Brilinta) at dose 180mg orally as a loading dose, followed by 90mg x BD for 12 months, then 60mg x BD if treatment is required beyond 12 months.
 - OR Tab. Clopidogrel 75mg (Ogrel, Plavix) at dose 300mg orally as a loading dose, followed by 75 mg once daily. Available combination: Aspirin 75mg/clopidogrel 75mg (Lowplat plus, Co-Plavix)
- Initial therapy for newly diagnosed patient without marked hyperglycemia/symptoms of catabolism (e.g., without polyuria, polydipsia, or unintentional weight loss) with HbA1c < 7.5

- Lifestyle modification: Exercise – increase physical activity, weight loss, balance diet and nutrition
- Anti-hyperglycemic management
 - Tab. Metformin 500mg, OR 850mg, OR 1000mg (Glucophage, Neophage) at dose 500mg two or three times daily with meals OR Tab. Glucophage 850mg – 1000mg x twice daily with breakfast and dinner
 - OR Tab. Metformin XR ^{Extended release} (Glucophage XR 500mg OR 750mg, OR 1000mg) x once daily
 - If contraindications to METFORMIN, we choose an alternative glucose-lowering medication guided by patient comorbidities, preferences, and cost: Empagliflozin, Semaglutide, Setagliptin OR Glimepiride
 - Dual therapy: When diabetes is not well controlled with initial therapy (usually METFORMIN) or HbA1c $\geq 7.5\%$, then add a second hyperglycemic agent (Empagliflozin, Semaglutide, Setagliptin OR Glimepiride).
 - Tab. Empagliflozin 10mg OR 25mg (Empaphage, Empagen, Emglip, Andrance) initially at dose 10mg orally once daily, increase according to response. **Maximum dose:** 25 mg/day.
 - OR Tab. Sitagliptin 50mg OR 100mg (Sitagen, Gvia, Trevia, Januvia) initially at dose 50mg orally once daily, increase according to response. **Maximum dose:** 100 mg/day.
 - OR Tab. Glimepiride 1mg OR 2mg OR 3mg OR 4mg (Amaryl, Glioptim, Evopride, Getryl) x initially dose at 1 – 4 mg once daily before breakfast. (ایک گولی صبح ناشتے سے پہلے). **Maximum dose:** 8mg/day.

» **AVAILABLE COMBINATION DUAL THERAPY:**

- » Tab. Empagliflozin + Metformin 12.5/500mg, 12.5/1000mg (Empagliflozin-M, Empagliflozin-M, Andranex-M)
- » OR Tab. Glimepiride + Metformin 1/500mg OR 2/500mg (Getformin, Evopride plus, Amaryl-M SR)
- » OR Tab. Sitagliptin+Metformin 50/500mg, 50/850mg, 50/1000mg (Sita-met, Sitagen-M, Treviamet)

1-0-1 (1 tablet two times a day with meal)

Patient without marked hyperglycemia/catabolism (e.g., without polyuria, polydipsia, or weight loss) with HbA1c <9% (<74.9 mmol/mol) or FBS <250 mg/dL (13.9 mmol/L), <300 mg/dL (16.7 mmol/L) or



1. Lifestyle modification: Exercise – increase physical activity, weight loss, balance diet and nutrition
2. Atherosclerotic Cardiovascular Disease (ASCVD) risk prevention/management as explained above
3. Anti-hyperglycemic management

» **Dual therapy:**

- » Tab. Empagliflozin + Metformin 12.5/500mg, OR 12.5/1000mg (Empagliflozin-M, Empagliflozin-M)
- » OR Tab. Glimepiride + Metformin 1/500mg, OR 2/500mg (Getformin, Evopride plus, Amaryl-M SR)
- » OR Tab. Sitagliptin+Metformin 50/500mg, OR 50/850mg, OR 50/1000mg (Sita-met, Sitaphage)

1-0-1 (1 tablet two times a day with meals)

» **Triple therapy: If targets are still not met despite adequate treatment: consider alternate oral glucose lowering agent with dual therapy OR add on GLP-1 receptor agonist**

- » Inj. Liraglutide (Victoza) at dose 0.6mg subcutaneously once daily initially, increase by 0.6mg/day increments at weekly intervals according to response. **Maximum dose:** 1.8 mg per 24 hours.
- » OR Inj. Semaglutide (Ozempic) at dose 0.25mg subcutaneously once weekly for 4 weeks initially, then increase to 0.5mg once weekly for at least 4 weeks, then may increase to 1mg once weekly for at least 4 weeks if response is inadequate, then may increase to 2mg once weekly if response is inadequate.
- » OR Tab. Semaglutide (Rybelsus) at dose 3mg orally once daily for 30 days initially, then increase to 7mg once daily for at least 30 days, then may increase to 14mg once daily if response is inadequate.
- » **Consider insulin therapy:** When the combination of oral agents (and injectable GLP-1 receptor agonists) fails to achieve euglycemia in patients with type 2 diabetes, then offer insulin as well for better control.

Patient with severe hyperglycemia or symptoms of catabolism with HbA1c ≥9% (≥74.9 mmol/mol), FBS >250 mg/dL (13.9 mmol/L), RBS consistently >300 mg/dL (16.7 mmol/L)



1. Lifestyle modification: Exercise – increase physical activity, weight loss, balance diet and nutrition
2. Atherosclerotic Cardiovascular Disease (ASCVD) risk prevention/management as explained above
3. Glycemic management:

- » **Continue the oral agents** (Metformin + DPP-4 inhibitors (Sitagliptin) ± SGLT2 inhibitors (Empagliflozin))
- » **Add Insulin therapy:** add simply bedtime dose insulin NPH OR Long-acting insulin analog (insulin glargine, detemir, or degludec) to reduce excessive nocturnal hepatic glucose output & improve fasting glucose levels.
 - » **Insulin NPH** (Insuget-N, Humulin-N) OR **Insulin glargine** (Lantus, Basagline, Lantus SoloStar, Toujeo SoloStar) OR **Insulin detemir** (Levemir, Levemir Flexpen) OR **Insulin degludec** (Ryzodeg Flexpen, Tresiba Flexpen) x 15 – 16 units x once daily at the same time each day, preferably at night.
 - » If the patient does not achieve target glucose levels during the day, then daytime insulin treatment can be initiated. A convenient insulin regimen under these circumstances is a split dose of 70/30 NPH/regular mixture (or Humalog Mix 75/25 or NovoLogMix 70/30) before breakfast and before dinner.
 - » If this regimen fails to achieve satisfactory glycemic goals or is associated with unacceptable frequency of hypoglycemic episodes, then a more intensive regimen of multiple insulin injections can be instituted as in patients with type 1 diabetes.
- » **±Add Glucagon-like peptide-1 (GLP-1) receptor agonist** (Liraglutide, Semaglutide) dosage as mention above.
 - » The ADA recommends that if insulin is used, combination therapy with a GLP-1 receptor agonist is used for greater efficacy, durability of treatment effect, and weight and hypoglycemia benefit.

N.B. » For patients presenting with severe hyperglycemia (FBS >250 mg/dL [13.9 mmol/L], RBS consistently >300 mg/dL [16.7 mmol/L], HbA1C >9% [74.9 mmol/mol]) but without ketonuria or spontaneous weight loss, in whom T1DM is not likely, we suggest insulin or a Glucagon-like peptide-1 (GLP-1) receptor agonist.

» For patients who are injection averse, initial therapy with high-dose sulfonylurea is an alternative, particularly for patients who have been consuming large amounts of sugar-sweetened beverages, in whom elimination of carbohydrates can be anticipated to cause a reduction in glucose within several days.

DIABETIC KIDNEY DISEASE (DKD)/DIABETIC NEPHROPATHY

- Introduction:** Diabetic kidney disease (DKD) is usually a clinical diagnosis in a patient with long-standing diabetes (>10 years) with albuminuria and/or reduced estimated glomerular filtration rate (eGFR) in the absence of signs or symptoms of other primary causes of kidney damage. Diabetic nephropathy remains the most common single cause of End-stage renal disease (ESRD)/End stage renal failure in 50% of the cases.
- Risk factors:** Sustained hyperglycemia, hypertension, family history of hypertension and/or kidney disease, obesity, smoking, physical inactivity, hyperlipidemia, high protein, fat, and sodium intake
- Pathophysiology:** Chronic hyperglycemia → glycation (also called non-enzymatic glycosylation or NEG) of the basement membrane (protein glycation) → increased permeability & thickening of the basement membrane and stiffening of the efferent arteriole → hyperfiltration (increase in GFR) → increase in intraglomerular pressure → progressive glomerular hypertrophy, increase in renal size, and glomerular scarring (glomerulosclerosis) → worsening of filtration capacity
- Pathology:** Three major histopathological changes can be seen on Light Microscope
1. Mesangial expansion
 2. Glomerular basement membrane thickening
 3. Glomerulosclerosis (Later stages)
 - » Diffuse hyalinization (most common) OR
 - » Pathognomonic nodular glomerulosclerosis (Kimmelstiel-Wilson nodules)
 - Glomerular capillary hypertension and hyperfiltration → Increase in mesangial matrix → eosinophilic hyaline material in the area of glomerular capillary loops
 - Can progressively consume the entire glomerulus → Hypofiltration (↓ GFR)

Diagnostic workup

- Urinalysis:** Proteinuria → hallmark of diabetic nephropathy is the development of proteinuria, which is due to alteration in glomerular basement membrane permeability and increases in intraglomerular pressure.
- Urine albumin/creatinine ratio (ACR):** moderately increased albuminuria: 30-299 mg/g; severely increased albuminuria: ≥300 mg/g. Collection of Early morning spot urine, collected upon awakening is preferred method
- BUN, serum creatinine and GFR calculation:** GFR may be elevated to normal in chronic kidney disease (CKD) stages 1-2 (≥60 mL/min/1.73 m²), and reduced in CKD stages 3-5 (<60 mL/min/1.73 m²)
- Kidney Ultrasound:** normal-to-large kidneys with increased echogenicity; may show hydronephrosis if vesiculopathy and/or obstruction is superimposed.
- Other test:** HbA1c, FBS, Fasting lipid profile (see diabetes mellitus as explain above)

CHRONIC KIDNEY DISEASE (CKD) CLASSIFICATION BASED UPON GFR & ALBUMIN EXCRETION RATE (AER)

Albuminuria stages	AER (mg/day)	Terms
» A1	<30	Normal to mildly increased (may be subdivided for risk prediction)
» A2	30 to 300	Moderately increased
» A3	>300	Severely increased (may be subdivided into nephrotic and non-nephrotic for differential diagnosis, management, and risk prediction)
GFR stages	GFR (mL/min/1.73 m ²)	Terms
» G1	≥90	Normal or high
» G2	60 to 89	Mildly decreased
» G3A	45 to 59	Mildly to moderately decreased
» G3B	30 to 44	Moderately to severely decreased
» G4	15 to 29	Severely decreased
» G5	<15	Kidney failure (add D if treated by dialysis)

DKD is assessed according to the presence of reduced estimated GFR and albuminuria. These factors are important predictors of CKD progression, cardiovascular disease, and mortality. **Abbreviation:** GFR: glomerular filtration rate; AER: albumin excretion rate; CKD: chronic kidney disease; KDIGO: Kidney Disease Improving Global Outcomes. DKD: Diabetes kidney disease

Data from:

KDIGO. Summary of recommendation statements. Kidney Int 2013; 3 (Suppl):5.
National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis 2002; 39 (Suppl 1):S1.

TREATMENT OF DIABETIC KIDNEY DISEASE (DKD)/DIABETIC NEPHROPATHY

Rx

- Lifestyle modification: Exercise – increase physical activity, weight loss, balance diet and nutrition
- Treatment of diabetes (Glycemic control):
 - » T1DM: In all type 1 diabetic patients, regardless of whether they are on dialysis or not, treatment with insulin is needed. Insulin is usually given subcutaneously. See T1DM above
 - » T2DM: Patients with type 2 diabetes and chronic kidney disease (CKD) who are not on dialysis may begin with First-line anti-hyperglycemic metformin if estimated GFR (eGFR) is ≥ 30 mL/min/1.73 m² and sodium-glucose cotransporter 2 (SGLT2) inhibitor to improve cardiovascular outcomes and limit CKD progression. Glucagon-like peptide 1 (GLP-1) receptor agonist is a reasonable second-line option.
 - ❖ Tab. Metformin 500mg, OR 850mg, OR 1000mg (Glucophage, Neophage) at dose 500mg two or three times daily with meals OR Tab. Glucophage 850mg – 1000mg x twice daily with breakfast and dinner.
 - ❖ + Sodium-glucose cotransporter 2 (SGLT2) inhibitors (Dapagliflozin, Canagliflozin, Empagliflozin), in addition to reducing hyperglycemia, have renal benefits through independent effects on renal tubular glucose reabsorption, weight, blood pressure, intraglomerular pressures, albuminuria & slowed GFR loss
 - » Tab. Dapagliflozin 10mg (Dapa, Xiga, Dapwiz) x Orally once daily
 - » OR Tab. Canagliflozin 100mg (Canliv) x Orally Once daily
 - » OR Tab. Empagliflozin 10mg OR 25mg (Empaphage, Empagen, Emglip, Andrance) initially at dose 10mg orally once daily, increase according to response. **Maximum dose:** 25 mg/day.
 - ❖ GLP-1 receptor agonist (Liraglutide, Semaglutide) if patient do not meet their individualized glycemic target with metformin &/or an SGLT2 inhibitor, or if these drugs are not tolerated/contraindicated.
 - ❖ DPP-4 inhibitors (Sitagliptin), can also be used, but the dose may need to be adjusted depending on the degree of renal dysfunction. Studies shows that this class may be Reno-protective but weak than SGLT2
 - ❖ Non-steroidal selective mineralocorticoid receptor antagonist (Finerenone): Among patients with T2DM who have measured or estimated albuminuria ≥ 30 mg/day despite an ACE inhibitor (or ARB) and an SGLT2 inhibitor (or if an SGLT2 inhibitor is not tolerated), we suggest treatment with Finerenone, where available. However, finerenone should generally be avoided in patients who have a serum potassium > 5 mEq/L or eGFR < 25 mL/min/1.73 m².
 - Treatment of hypertension reduces progression of DKD: Angiotensin converting enzyme (ACE) inhibitors OR Angiotensin receptor blockers (ARBs) have been shown to delay the progression of diabetic nephropathy & are recommended for patients with albuminuria even in the absence of hypertension. **Combination therapy with both an ACE inhibitor and an ARB, or combining one of these drugs with a renin inhibitor, should be avoided.**
 - » Angiotensin converting enzyme (ACE) inhibitors: dose should be adjusted according to level of renal impairment
 - ❖ Tab. Captopril 25mg OR 50mg OR 20mg (Capoten, Capril, Acetopril) at initially dose 25mg orally three times daily, increase gradually according to response. **Maximum:** 450mg mg/day.
 - ❖ OR Tab. Enalapril 5mg OR 10mg OR 20mg (Renitec, Cardace, Cortec) at initially dose 2.5-5mg x orally once daily, increase gradually according to response. **Maximum:** 40 mg/day.
 - ❖ OR Tab. Lisinopril 5mg OR 10mg OR 20mg (Zestril, Lispril, Lame) at initial dose 2.5-5mg x orally once daily, increase gradually according to response. **Maximum:** 40 mg/day.
 - ❖ OR Tab. Ramipril 2.5mg OR 5mg OR 10mg (Tritace, Ramipace) at initially dose 2.5-5mg x orally once daily, increase gradually according to response. **Maximum:** 20 mg/day.
 - » OR Angiotensin receptor blockers (ARBs)
 - ❖ Tab. Candesartan 8mg OR 16mg (Advant, Canrec, CanSaar) at initially dose 4mg-8mg x orally once daily, increase gradually according to response. **Maximum:** 32 mg/day.
 - ❖ OR Tab. Valsartan 80mg OR 160mg (Diovan, Nobel, Exforge) at initially dose 40mg-80mg x orally once daily, increase gradually according to response. **Maximum:** 320 mg/day.
 - ❖ OR Tab. Losartan 25mg OR 50mg OR 100mg (Eziday, Sartan) at dose 25 mg orally once daily initially, increase gradually 50mg according to response. **Maximum:** 100 mg/day.
 - » With Blood pressure not controlled $< 130/80$ mmHg by ACE inhibitor/ARBs: Consider CCBs (Amlodipine) and/or thiazide diuretics (Hydrochlorothiazide) and/or beta-blockers (Bisoprolol) – see hypertension
 - Lipid control management → initiate moderate intensity statins
 - » Tab. Atorvastatin 10mg OR 20mg (Statin, Lipitor) at dose 10-20 mg x orally x once daily (OD)
 - » OR Tab. Fluvastatin 20mg OR 40mg (Lescol) at dose 20-40mg BD; or Lescol XR 80mg (extended-release) x orally OD
 - » OR Tab. Rosuvastatin 5mg OR 10mg (Crestor, X-Plended) at dose 5-10 mg x orally once daily



DIABETIC NEUROPATHY

- **Definition:** Diabetic neuropathy is a highly prevalent chronic complication of diabetes mellitus type 1 or type 2 and is characterized by the presence of symptoms and/or signs of peripheral nerve dysfunction and/or autonomic nerve dysfunction, which results from hyperglycemia-induced metabolic vascular, and molecular derangements.
- **Epidemiology:** Diabetic polyneuropathy is the most common form of polyneuropathy, ~ 50% of patients with diabetes develop peripheral neuropathy & 90% of patients with diabetes may develop autonomic neuropathy
- **Risk factors:** Poorly controlled hyperglycemia, prolonged duration of hyperglycemia, older age >70 years of age, tall stature, hypertension, obesity, smoking, hyperlipidemia with elevated triglycerides, co-existence of multiple CVD risk factor, immune dysregulation and genetic.
- **Pathophysiology** involves complex mechanisms, including oxidative stress, advanced glycation end products, microvascular damage, and altered nerve cell metabolism → nerve damage, inflammation, and cell death.
- **Diabetic peripheral neuropathy**
 - » **Types:**
 - ↳ **Diabetic distal symmetric polyneuropathy**
 - ↳ **Isolated peripheral neuropathy:** Mononeuropathy (only one nerve affected (e.g., carpal tunnel syndrome [median nerve], foot drop [common peroneal nerve]), mononeuropathy multiplex: asymmetric neuropathy, affecting the multiple peripheral and cranial nerves (cranial neuropathies are extremely rare)
 - ↳ **Diabetic radioculoplexus neuropathy:** most commonly diabetic lumbosacral plexopathy/Diabetic truncal radiculoneuropathy (pain over the lower thoracic or abdominal wall)
 - » **Clinical features:** Many individuals with diabetic peripheral neuropathy are asymptomatic and the condition is often detected only during screening or after complications develop.
 - ↳ **Sensory symptoms:** Distal symmetrical sensory loss (stocking glove sensory loss pattern with proximal progression), numbness, tingling, dysesthesia (e.g., burning feet syndrome with symptoms that worsen at night, pain at rest and at night) and less common features (allodynia, hyperesthesia)
 - ↳ **Motor weakness:** e.g., muscle weakness (not fatigue), ataxic gait, balance problems
 - ↳ **Neurological examination may show loss or reduction of:** Ankle reflex, vibration sense (using a tuning fork), sharp/dull discrimination (e.g., pinprick sensation), light touch (e.g., monofilament test), proprioception and reduction of temperature sensation
- **Diabetic autonomic neuropathy:**
 - » Occurs principally in patients with diabetes of long duration due to damage to small fiber autonomic nerves; multiple organ systems are susceptible. It affects many diverse visceral functions including blood pressure and pulse, gastrointestinal (GI) activity, bladder function, and sexual dysfunction.
 - » **Insulin neuritis or treatment induced neuropathy** in diabetes occurs occasionally in patients who have had poor glucose control and then whose glucose levels improve rapidly in days or a few weeks.
 - » **Clinical features:**
 - ↳ **Genitourinary autonomic neuropathy:**
 - **Sexual dysfunction:** erectile dysfunction, loss of libido, dyspareunia, vaginal dryness, anorgasmia
 - **Neurogenic bladder:** urinary retention, incomplete bladder emptying, bladder distention overflow incontinence, poor urinary stream
 - ↳ **Cardiovascular autonomic neuropathy:** Exercise intolerance, fatigue, sustained heart rate, syncope, dizziness, lightheadedness, balance problems, orthostatic hypotension, tachycardia at rest
 - ↳ **Gastrointestinal autonomic neuropathy:** Diabetic gastroparesis (dysphagia, bloating, nausea and vomiting, diarrhea, constipation, loss of bowel control [fecal incontinence])
 - ↳ **Sudomotor (sweat gland) dysfunction:** Pruritis, dry skin, heat intolerance, abnormal sweating (e.g., anhidrosis, gustatory sweating)
 - ↳ **Endocrine symptoms:** hypoglycemia unawareness
 - ↳ **Other symptoms:** Difficulty driving at night, depression, anxiety, sleep disorders, cognitive changes



Plantar ulcer in a patient with T1DM



Charcot foot in a patient with diabetes



Superficial ulcer in a patient with diabetes





Plantar ulcer in a patient with T1DM



Plantar foot ulcer on the fifth metatarsal head.



Diabetic foot ulcers

Diagnostic workup

- Diabetic neuropathy is often a clinical diagnosis on the basis on clinical symptoms and examination
- History:** Review diabetes history, disease management, daily glycemic records, and previous HbA1c levels.
- Perform a focused history based on the suspected affected organ.**
- Basic laboratory tests include:** CBC, LFTs, Fasting lipid profile, Fasting blood glucose (FBS), HbA1c, and 75g OGTT, serum TSH, vitamin B12, BUN & creatinine, ESR and Hb electrophoresis.
- Obtain investigation as needed to rule out alternative etiologies and confirm the diagnosis.**
- » **Diabetic peripheral neuropathy:**
 - ↳ **Electrophysiologic testing:** can help identify and localize nerve dysfunction, but often do not reveal the underlying cause of neuropathy.
 - **Nerve conduction tests**
 - Demyelinating disease: ↓ impulse conduction velocity, normal amplitude of response
 - Axonal disease: normal impulse conduction velocity, ↓ amplitude of response
 - **Electromyography (EMG):** Can differentiate between neuropathy and myopathy, Polyneuropathy findings may include spontaneous electrical activity (fibrillation potentials) and reduced interference pattern.
 - **Quantitative sensory testing**
 - ↳ **Additional testing:**
 - **MRI brain:** patients with cranial nerve palsies, ataxia, or dysarthria
 - **MRI spine:** patients with suspected radiculopathy
 - **MR Neurography:** may be considered in atypical neuropathies.
 - **Sural nerve biopsy:** performed in diagnostic uncertainty or prior to starting aggressive treatments
 - **Skin biopsy:** may be performed in patients with a burning sensation or painful neuropathy
 - **CSF analysis:** for suspected infections or chronic inflammatory demyelinating polyneuropathy
- » **Diabetic Autonomic neuropathy:**
 - ↳ **Genitourinary studies**
 - Urodynamic testing to assess for neurogenic bladder dysfunction (Urine culture, Postvoid ultrasound, Cystometry, voiding cystometrogram and Video-urodynamic studies
 - Early morning (8.00-9.00 a.m.) hormonal evaluation (luteinizing hormone, testosterone, prolactin) to rule out hypogonadism or sexual dysfunction (Erectile dysfunction)
 - Measurement of nocturnal penile tumescence, measurement of penile and brachial BP with Doppler probes for Erectile dysfunction
 - ↳ **Cardiovascular studies**
 - **Orthostatic vital signs:** to assess for orthostatic hypotension → Respiratory rate [RR] response to deep breathing (Diagnostic in 80%), Valsalva maneuver, and RR response to postural changes
 - **ECG:** to assess for resting tachycardia and decreased HR variability
 - ↳ **Gastrointestinal (GI) studies**
 - **Stool investigation in patients with diarrhea:** Stool D/R, Stool culture
 - **Esophageal barium swallow:** to assess for esophageal hypermotility disorders
 - **Upper gastrointestinal endoscopy:** to rule out gastric outlet obstruction and peptic ulcer disease
 - **Colonoscopy:** in case of diarrhea or red flags in patients with constipation
- » **Additional laboratory tests:** Perform based on clinical suspicion if indicated.
 - » **Infections workup:** HBsAg, Anti-HCV, HIV screening, Lyme ELISA, Syphilis screening
 - » **Serum ACE levels for Sarcoidosis**
 - » **Autoimmune or inflammatory disease:** ESR, CRP, ANA, c-ANCA, p-ANCA (Specially in D1DM)

TREATMENT OF DIABETIC NEUROPATHY

- Lifestyle modification: Exercise – increase physical activity, weight loss, balance diet and nutrition.
- Counseling: Educate patients and caregivers on measures to prevent complications, diabetic foot care.
- Glycemic control: Optimize diabetes management to achieve glycemic targets in DM – see T1DM or T2DM.
- If possible, discontinue medications that may contribute to symptoms.
- Treat dyslipidemia and hypertension, if present.
- Treatment varies depending on the organ system(s) affected:
 - **Treatment of diabetic peripheral neuropathy:** Provide pain relief, if necessary, Follow up with patients regularly; adjust medication if pain remains inadequately controlled after 12 weeks of use.
 - Cap. Pregabalin 50mg OR 75mg OR 100mg (Gabica, Prelin, Syngab) at dose 50-100 mg orally three times daily initially, increase gradually according to response, maximum 600 mg/day
 - OR Cap. Duloxetine 30mg OR 60mg (Lyta, Dulan, Cymbalta) initially at dose 30-60mg orally once daily
 - OR Cap. Gabapentin 300mg OR 600mg (Gabix, Neogab) initially at dose 300mg orally three times daily, increase by 300mg/day increments at weekly intervals according to response, maximum: 3600mg/day
 - OR If no response then combine therapy: Pregabalin or Gabapentin PLUS Duloxetine
 - OR Tab. Amitriptyline 25mg (Tryptanol) initially at dose 12.5-25 mg orally once daily at bedtime, increase according to response, maximum 150 mg/day, it has more anticholinergic effects
 - ± Short-term OPIATES:
 - Tab. Tramadol 50mg OR 100mg (Tramal, Tonoflex) 50 – 100 mg x TID (Maximum: 400mg/day)
 - OR Tab. Tapentadol 50mg OR 75mg (Tapento IR, Tydel) at dose 50 – 75 mg x TID (Maximum: 500mg/day)
 - Capsaicin 0.025% cream (0.075%) applied sparingly 3 – 4 times per day OR Capsaicin 8% patch plaster
 - Consider multivitamins supplementation if deficient: Folic acid, Vitamin B12, phosphorus, thiamine
- **Treatment of diabetic autonomic neuropathy:**
 - Treatment of bladder dysfunction: see urology section – urinary incontinence for detail management
 - Tab. Bethanechol 10-30 mg orally three times daily
 - Bladder hygiene technique: Bladder training, such as scheduled voiding, may be used particularly for urge incontinence. The Crede maneuver may also be used. This method helps to empty the bladder if it is weak and flaccid. The patient pushes with a hand down on the abdomen from the umbilicus toward the bladder in a smooth, even manner.
 - Treatment of Sexual dysfunction: see urology section– erectile dysfunction for detail management
 - Tab. Sildenafil (Viagra) at dose 25-100mg orally taken 1 hour before anticipated sexual activity
 - OR Tab. Tadalafil (Cialis) at dose 5-20mg orally taken 45 minutes before anticipated sexual activity
 - Symptoms of diabetic gastroparesis:
 - Tab. Erythromycin 250mg (Erythrocin) orally 4 times daily 30min before meals and at bedtime
 - OR Tab. Metoclopramide 10mg (Metaclo, Maxolon) at dose 5-10mg orally three times daily for a maximum of 5 days, maximum 30mg/day.
 - OR Onabotulinumtoxin-A (formerly known as botulinum toxin type-A) intrapyloric injection during upper gastrointestinal endoscopy (upper EGD).
 - Diabetic diarrhea: Diarrhea associated with autonomic neuropathy has occasionally responded to broad-spectrum antibiotic therapy (such as Rifaximin, Metronidazole, Ciprofloxacin, or Doxycycline)
 - Tab. Rifaximin 550mg (Rifixa, Nixaf) orally three times daily for 2 weeks
 - OR Tab. Metronidazole 500mg (Flagyl, Klint) orally every 6 hours for 3 weeks
 - ± Cap. Loperamide 2mg (Imodium, Floramex) orally three to four times daily
 - Manage orthostatic hypotension.
 - Non-pharmacological management of orthostatic hypotension and syncope, including regular exercise, use of Jobst fitted stockings, tilting the head of the bed, and arising slowly from the supine position can be helpful in treating symptoms of orthostatic hypotension.
 - Pharmacological treatment:
 - Tab. Midodrine 5mg at dose 2.5 to 10 mg orally three times daily
 - OR Tab. Fludrocortisone 0.1mg (Flurocort, Florinef) at dose 0.1 to 0.2 mg orally once daily
 - Use of short-acting drugs at bedtime for patients with supine hypertension



DIABETIC RETINOPATHY

- **Epidemiology:** After 15 years with prolonged disease, approximately 80% of T1DM patients and approximately 30% of T2DM patients develop diabetic retinopathy. Diabetic retinopathy is the most common cause of visual impairment and blindness in patients aged 20 – 75 years.
- **Risk factors:** Poorly controlled hyperglycemia, prolonged duration of diabetes, presence of diabetic nephropathy, hypertension, obesity, smoking, dyslipidemia, pregnancy and history of cataract surgery
- **Ophthalmological findings and classification of diabetic retinopathy**
 - » **Non-proliferative retinopathy (NPDR):** accounts for most cases of diabetic retinopathy
 - ↳ **Exam findings:** Microaneurysms, caliber changes in venous vessels, intraretinal hemorrhage, hard exudates, retinal edema, cotton-wool spots and intraretinal microvascular abnormalities (IRMA)
 - ↳ **Vision loss:** Most commonly due to macular edema
 - » **Proliferative retinopathy (PDR)**
 - ↳ **Exam findings:**
 - Findings of nonproliferative retinopathy are usually present.
 - Neovascularization is the hallmark of proliferative retinopathy (PDR)
 - Fibrovascular proliferation; vitreous hemorrhage, traction retinal detachment
 - Rubeosis iridis → secondary glaucoma.
 - ↳ **Vision loss:** May be due to vitreous hemorrhage, retinal detachment, or neovascular glaucoma.
 - » **Macular edema**
 - ↳ **Exam findings:** clinically significant retinal thickening and edema involving the macula, hard exudates, macular ischemia. May occur in all stages of NPDR and proliferative retinopathy (PDR)
 - ↳ **Vision loss:** May lead to vision loss
- **Diagnostic workup:** Usually detected on screening, symptomatic patients should undergo a comprehensive eye examination (including slit lamp examination and fundoscopy) with the pupil dilated. **Ancillary testing**, e.g., optical coherence tomography (OCT), fluorescein angiography and digital photographs of the fundus may be indicated.



TREATMENT OF DIABETIC RETINOPATHY

- Early referral all patients with diabetic retinopathy to an ophthalmologist for evaluation: need
- **Lifestyle modification:** Exercise – increase physical activity, weight loss, balance diet and nutrition.
- **Glycemic control:** Optimize diabetes management to achieve glycemic targets in DM – see T1DM or T2DM.
- **Atherosclerotic Cardiovascular Disease (ASCVD) risk prevention/management:** explained above – see T2DM
- **Treatment by retinopathy subtype:**
 - » **Nonproliferative retinopathy (NPDR)**
 - ↳ **Mild NPDR to moderate NPDR:** Observation only; repeat dilated comprehensive eye examination every 6–12 months.
 - ↳ **Severe NPDR:** Treat as proliferative retinopathy with **panretinal laser photocoagulation (PRP)** &/or **Intravitreal anti-vascular endothelial growth factor (VEGF) therapy**
 - **Aflibercept intravitreal** at dose 2 mg intravitreally into the affected eye(s) every 4 weeks for 5 doses, followed by 2 mg every 8 weeks
 - **Ranibizumab intravitreal** at dose 0.3 mg intravitreally into the affected eye(s) once monthly
 - » **Proliferative retinopathy (PDR):** PRP and/or anti-VEGF therapy
 - ↳ Both PRP and anti-VEGF therapy are equally effective.
 - ↳ PRP is usually preferred as treatment occurs in a single session (reduces risk of loss to follow-up)
 - ↳ Anti-VEGF injections alone can be considered for patients who are highly motivated and have no barriers to follow-up.
 - » **Treatment of macular edema**
 - ↳ **Center-involving diabetic macular edema**
 - **First line:** Intravitreal anti-VEGF therapy
 - Consider PRP or focal and/or grid laser depending on severity of retinopathy.
 - ↳ **Noncenter-involving diabetic macular edema:** PRP, anti-VEGF, or focal and/or grid laser therapy may be used depending on severity of retinopathy.
 - » **Refractory disease or severe complications** (e.g., tractional retinal detachment, vitreal hemorrhage)
 - Consider **vitrectomy:** surgical procedure to remove hemorrhage & scar tissue that is obscuring vision

NON-INSULIN ANTIDIABETICS/ANTI-HYPERGLYCEMIC DRUGS

GENERIC	BRAND & AVAILABLE STRENGTH	DAILY DOSAGE
SULFONYLUREAS		
Glibenclamide Glipizide	Tab Daonil 5mg Tab Euglucon 5mg Tab Minidiab 5mg	Usual dose is 5 mg 2 times daily, start with low dose, Maximum dose: 20mg per day Usual dose: 2.5–10mg x BD 30 min before meals Maximum dose: 20 mg twice daily
	Tab Diamicon 80mg Tab Diabetron 80mg Tab Diamicon MR 30mg, MR 60mg Tab Scicon MR 30mg or MR 60mg	Daily dose: 40–80 mg as single dose 160–320 mg as divided dose
	Tab Amaryl, Tab Evopride Tab Glioptim, Tab Diatrol Available strength: 1mg, 2mg, 3mg, 4mg	Usual dose: 1–4 mg once daily Maximum dose: 8 mg once daily
BIGUANIDES		
Metformin	Tab Glucophage Tab Neophage Strength available: 250mg, 500mg, 850mg and 1000mg	Daily dose: 500–850mg with meals two or three times daily; 850–1000mg with breakfast & dinner
	BIGUANIDES + SULFONYLUREAS	
Metformin + Glibenclamide	Tab Glucovance 500mg/2.5mg Tab Glucovance 500mg/5mg	One tablet 2 times a day with meal
Glipizide + Metformin	Tab Minidiab AF 2.5/500mg, Tab Minidiab AF 5mg/500mg	One tablet 2 times a day with meal
Glimepiride + Metformin	Tab Amaryl-M SR Tab Evopride plus Tab Getformin Available strength: 1/500mg, 2/500mg	One tablet once a day before or with breakfast or first main meal. Then titrate gradually as needed.
	MEGLITINIDE ANALOGS	
Repaglinide	Tab Repag 0.5mg, 1mg, 2mg Tab Raptrol 0.5mg, 1mg, 2mg	Usual dose: 0.5 to 4mg x TID 15 min before meals. Maximum dose: 16 mg daily
d-PHENYLALANINE DERIVATIVE		
Nateglinide	Tab Glytan 60mg, 120mg	Daily dose: 60 or 120mg x TID before meals
GLP-1 RECEPTOR AGONISTS		
Dulaglutide	Inj. Trulicity 0.25mg/0.5ml, 0.75mg/0.5ml or 1.5mg/0.5ml	Usual dose: 0.75 mg subcutaneously once weekly Maximum dose: 1.5mg x SC, once weekly
Liraglutide x SC	Inj. Victoza 6mg/ml Inj. Saxenda 6mg/ml	Initial dose: 0.6mg subcutaneously once daily. Increase to 1.2mg after a week if no adverse reactions. Maximum dose: 1.8mg x SC, OD
Semaglutide x SC	Inj. Ozempic 0.25mg, 0.5mg, 1mg or 2mg	Initial dose 0.25mg x SC, weekly for 4 weeks, then increase to 0.5mg once weekly for at least 4 weeks, then may increase to 1mg once weekly for at least 4 weeks if response is inadequate, then may increase to 2mg once weekly.
Semaglutide x Orally	Tab. Rybelsus 3mg, 7mg, 14mg	Initial dose: 3mg x OD for 1 month 30 min before meal, then increase to 7mg x OD for at least 1 month. Maximum: 14mg per day
DUAL GIP/GLP-1 RECEPTOR AGONISTS		
Tirzepatide x SC	Inj. Mounjaro 2.5, 5, 7.5, 10, 12.5, and 15 mg	Initial dose: 2.5mg weekly for 1 month and increase to 5mg weekly. Increase dose by 2.5 mg weekly at 1-month intervals for additional glucose lowering. Maximum dose: 15 mg weekly
THIAZOLIDINEDIONES		
Rosiglitazone	Tab Rosita 2mg, 4mg and 8mg Tab Rosiscot 2mg, 4mg	Daily dose: 4–8 mg daily (can be divided)



Pioglitazone	Tab Piozer, Tab Zolid Available strength: 15mg, 30mg, and 45mg	Daily dose: 15-45 mg daily
BIGUANIDES + THIAZOLIDINEDIONES		
Pioglitazone + Metformin	Tab Piozer plus Tab Zolid plus Available strength: 15/500mg, 15/850mg	One tablet 2 times a day with meal
Pioglitazone + Glimepiride	Tab Piozer-G Tab Zoliget Available strength: 30/2mg, 30/4mg	Initially, one tablet once daily then titrate gradually as needed.
ALPHA-GLUCOSIDASE INHIBITORS		
Acarbose	Tab Glucobay 50mg, OR 100mg	Daily dose: 25-100mg x TID just before meals
DIPEPTIDYL PEPTIDASE-4 INHIBITOR (DPP4 INHIBITORS)		
Sitagliptin	Tab Gvia 50mg, 100mg Tab Trevia 50mg, 100mg Tab Sita 50mg, 100mg	100mg OD, if eGFR > 50 mL/min/1.73 m ² 50mg OD, if eGFR 30-50 mL/min/1.73 m ² 25mg OD, if eGFR < 30 mL/min/1.73 m ²
Linagliptin	Tab Tradjenta 5 mg Tab Lina 5mg	5 mg once daily
Vildagliptin	Tab Vilget 50mg Tab Viglip 50mg Tab Galvecta 50mg	50 mg once or twice daily. AVOID if eGFR ≤ 60 mL/min/1.73 m ² or AST/ALT three times upper limit of normal
Saxagliptin	Tab Onglyza 2.5mg, and 5mg Tab Saxagen 2.5mg and 5mg	2.5 mg or 5 mg once daily if eGFR > 50 mL/min/1.73 m ² . 2.5 mg daily if eGFR ≤ 50 mL/min/1.73 m ² or if also taking drugs that are strong CYP3A4/5 inhibitors such as ketoconazole
BIGUANIDES + DPP-4 INHIBITORS		
Sitagliptin + Metformin	Tab Sita-met, Tab Sitaphage Tab Gvia-M, Tab Trevia-met Available strength: 50/500mg, 50/850mg, 50/1000mg	One tablet 2 times a day with meal
Vildagliptin + Metformin	Tab Vilget-M, Tab Viglip-M Available strength: 50/500mg, 50/850mg, 50/1000mg	One tablet 2 times a day with meal
SGLT2 INHIBITORS		
Dapagliflozin	Tab Dapa 5mg, and 10mg Tab Dapwiz 5mg, and 10mg Tab Xiga 5mg, and 10mg	Daily dose: 10mg daily
Empagliflozin	Tab Empagen 10mg and 25mg Tab Empaphage 10mg and 25mg Tab Andrance 10mg and 25mg	Usual dose: 10 mg daily Maximum dose: 25 mg
Canagliflozin	Tab Canliv 100mg	Usual dose: 100 mg daily. Can use 300 mg daily if normal eGFR, resulting in lowering the HbA1c an additional ~ 0.1-0.25%.
Ertugliflozin	Tab Ertuvia 5mg, and 15mg Tab Ertuget 5mg, and 15mg	AVOID if eGFR < 45 mL/min/1.73 m ² Usual dose: 5 mg daily
Sotagliflozin	Tab Inpefa 200mg	Maximum dose: 15 mg 200mg increased up to 400mg once daily
SGLT2 INHIBITORS + DPP4 INHIBITORS		
Ertugliflozin + Sitagliptin	Tab Ertuvia-S 5/100mg, 15/100mg Tab Trevia R2 5/100mg, 15/100mg	One tablet once daily, taken in the morning, with or without food
Linagliptin + Ertugliflozin	Tab Empagen-L 5/10mg, 5/25mg Tab Linjardy 5/10mg, 5/25mg	
BIGUANIDES + SGLT2 INHIBITORS		
Dapagliflozin + Metformin	Tab Dapa-met Tab Dapalozmet Available strength: 5/850mg, 5/1000mg	One tablet 2 times a day with meal
Empagliflozin + Metformin	Tab Empagen-M Tab Empaphage-M Tab Empozin-M Available strength: 5/500mg, 5/850mg, 5/1000mg, 12.5/500mg, 12.5/1000mg	One tablet 2 times a day with meal

INSULIN REGIMENS

- Insulin regimens should be tailored individually to each patient.
- There are a variety of options for patients with T2DM.
- Treatment of T1DM requires intensive insulin therapy with a multi-injection regimen or insulin pump.

Basal insulin regimens

- Description:** Basal insulin is added to an oral antidiabetic drug regimen.
- Indication:** Type-2-DM with persistently elevated Hb A1C levels despite adequate treatment with non-insulin antidiabetics
- Treatment options**
 - Once-daily injection (recommended starting regimen)**
 - Long-acting insulin (e.g., glargine) OR bedtime NPH insulin
 - Starting dose:** 10 units/day OR 0.1–0.2 units/kg/day
 - Twice-daily NPH insulin:** Consider for patients not meeting their glycemic target with bedtime NPH.
 - Starting dose:** 80% of the previously prescribed bedtime NPH insulin dose, with two-thirds given in the morning and one-third at bedtime
- Titration**
 - Adjust according to glycemic monitoring.
 - Levels above target:** Increase insulin dose by 2 units every 3 days until preprandial fasting glucose target is met.
 - If hypoglycemia due to insulin therapy occurs, reduce insulin dose by 10–20%.
 - If treatment remains insufficient despite appropriate adjustments, intensify treatment by either adding prandial insulin or considering a mixed regimen.

CAUTION: Not all noninsulin antidiabetics can be combined with insulin. Combination therapy with insulin and sulfonylureas should be avoided because of the risk of hypoglycemia and increased mortality! Once insulin is started, consider tapering and eventual discontinuation of sulfonylureas. Insulin combined with pioglitazone increases the risk of edema, weight gain, and congestive heart failure. Metformin is usually continued.

Addition of prandial insulin

- Description**
 - Short-acting insulin or rapid-acting insulin is injected before major meals in patients already on a basal insulin regimen.
 - Prandial insulin can be added before one meal (the largest meal of the day) or several meals.
- Indication:** T2DM that is not adequately controlled with basal insulin alone
- Starting dose**
 - Basal insulin injections are continued at the previous dose.
 - 4 units of short-acting or rapid-acting insulin before chosen meals
- Titration:** Adjust according to glycemic monitoring.
 - Increase prandial insulin dose by 1–2 units twice weekly until preprandial fasting glucose target is met.
 - If hypoglycemia occurs, reduce the corresponding prandial insulin dose by 10–20%.

Mixed insulin regimens

- Description**
 - Twice-daily injections of a fixed combination of NPH mixed with either short-acting insulin or rapid-acting insulin; can be self-mixed or premixed
 - Simple regimens that require minimal patient education and time
- Indication:** Consider for patients with T2DM who are not meeting glycemic targets with a basal insulin regimen.
- Starting dose**
 - Self-mixed insulin**
 - Calculate 80% of the current NPH dose.
 - Add 4 units of short-acting or rapid-acting insulin per injection.
 - Premixed insulin:** Use the same previous total insulin dose (i.e., the same as for the twice-daily NPH regimen).
- Titration**
 - Adjust according to glycemic target.
 - If treatment results remain inadequate, consider a full basal-bolus regimen.

Principles of insulin adjustment

- ☐ **Preprandial glucose**
 - » Mainly affected by the basal insulin dose
 - » Daily capillary early morning measurements & measurements before applying an insulin dose are advised.
- ☐ Postprandial glucose is mainly affected by meal intake and prandial insulin dose.
- ☐ Certain conditions require temporary insulin adjustments.
 - » **Increased insulin demand**
 - Illness
 - Stress
 - » **Decreased insulin demand**
 - Physical activity
 - Vomiting and diarrhea: can lead to decreased glucose uptake, increasing the risk of hypoglycemia
 - Fasting, e.g., for surgery

Sliding-scale insulin regimen

- ☐ Sliding-scale insulin regimens vary and institutional standards should be followed. Sliding-scale regimens alone should not be used for the long-term management of diabetes.
- ☐ **If the patient is eating all or most of each meal:** Administer as short-acting insulin (or rapid-acting insulin) before each meal and at bedtime.
- ☐ **If the patient is not eating:** Administer as short-acting insulin every 6 hours.
- ☐ If blood glucose is < 70 mg/dL, hold all insulin and administer measures to control hypoglycemia.

Example of administration of sliding scale insulin

Blood glucose (mg/dL)	Insulin units		
	Insulin sensitive	Usual insulin	Insulin resistant
71 – 140 mg/dL	0	0	0
141 – 180 mg/dL	2	4	4
181 – 220 mg/dL	4	6	8
221 – 260 mg/dL	6	8	10
261 – 300 mg/dL	8	10	12
301 – 350 mg/dL	10	12	14
351 – 400 mg/dL	12	14	16

Insulin regimens for Glucocorticoid-Induced Hyperglycemia

- ☐ **Basal-bolus insulin regimen (preferred)**
 - » Consider splitting the total daily dose of insulin 30/70 (i.e., 30% long-acting insulin and 70% prandial short-acting insulin).
 - » Patients usually require about 0.4 units/kg/day but in patients receiving dexamethasone, insulin doses as high as 1.0–1.2 units/kg/day may be necessary.
 - » The total required insulin dosage depends on individual patient factors (e.g., prior insulin sensitivity) and the potency of the steroid.
- ☐ **Sliding-scale insulin regimen:** may be adequate for short-term management
- ☐ **Weight-based NPH insulin regimen**
 - » Convert glucocorticoid to equivalent prednisolone dose
 - » Calculate daily NPH dose based on prednisone dose equivalent and patient weight.
 - » Administer glucocorticoid with NPH as a single dose in the morning.

Prednisolone dose equivalent (mg/day)	NPH (units/kg/day)
10	0.1 units/kg/day
20	0.2 units/kg/day
30	0.3 units/kg/day
≥ 40	0.4 units/kg/day

DIABETIC KETOACIDOSIS (DKA)

Name: _____ Age: _____ Sex: _____ Date: _____
 Temperature: _____ B.P: _____ Pulse: _____ Resp. Rate: _____

CLINICAL PRESENTATION OF DKA:

- ✓ Rapid onset (<24hr) in contrast to HHS (Insidious/days)
- ✓ Classic features of DM: Polydipsia, Polyuria.
- ✓ Sign of dehydration (Dry mucous membranes, decreases skin turgor), hypotension, and shock.
- ✓ Hyperventilation: rapid deep breathing (Kussmaul Respirations)
- ✓ "Fruity" breath odor of acetone (nail polish remover smell in the breath) strongly suggest the diagnosis
- ✓ Hyperviscosity Syndrome:
 - » CNS features: ASOC, Lethargy, drowsiness, confusion, coma, convulsions and CVA.
 - » Eyes features: Blurring of vision
 - » Cardiovascular features: Angina, myocardial infarction, ischaemic heart disease (IHD)
 - » Gastrointestinal tract features: Epigastric pain, mesenteric ischaemia → acute abdominal pain (according to the area of vessel involvement, abdominal tenderness, Nausea and vomiting.

DIAGNOSTIC APPROACH

- ✓ Check Blood sugar level (BSL): > 250 mg/dL (> 13.9 mmol/L)
 About 10% of patients with DKA will be euglycemic (e.g., glucose ≤ 250 mg/dL)
- ✓ Elevated Serum BUN (Blood, urea, nitrogen) and serum creatinine level
- ✓ Serum electrolytes: deranged
- ✓ Check Anion gap = $(Na^+ + K^+) - (Cl + HCO_3^-)$ or $Na^+ - (Cl + HCO_3^-)$
- » Normal value 10-12 mmol/L, Anion gap will be high in DKA
- ✓ Check for the presence of ketones in urine (ketonuria) → test urinalysis.
- ✓ Serum beta-hydroxybutyrate: > 4 nl/L (B-hydroxybutyrate most common ketone produced in DKA. Serum measurement is more sensitive than urine ketone)
- ✓ Check ABGs: high anion gap metabolic acidosis
 - » Severe acidosis: pH ranging from 6.9 to ≤ 7.30
 - » Serum bicarbonate (HCO_3): value may be ranging from 5 mEq/L to 15 mEq/L
 - » pCO_2 : Low 15 to 20 mmHg, related to compensatory hyperventilation
- ✓ Diagnostic workup to evaluate the underlying cause: HbA1c, CBC, serum LDH, LFTs, serum amylase and serum lipase, serum procalcitonin, blood culture, urine culture.
- ✓ Radiology if indicated: CT scan abdomen, Chest X-ray and ECG.

DIAGNOSTIC CRITERIA

- ✓ Hyperglycemia: Blood sugar level > 250 mg/dL
- ✓ Ketonuria: Moderate to large urine ketones
- ✓ Ketonemia: Positive blood ketone
- ✓ Acidosis: Blood pH < 7.3
- ✓ Serum bicarbonate: < 18 mmol/L

DKA VS HHS

- ✓ DKA: hyperglycemia, high anion gap metabolic acidosis, ketonuria/ketonemia
- ✓ Hyperosmolar hyperglycemic state (HHS): Hyperglycemia, hyperosmolality, and dehydration without ketonuria, Also known as Hyperosmolar Non-ketotic coma (HONK)

Formula for Hyperosmolarity = $2(Na + K) + \frac{BUN}{2.8} + \frac{BSL}{18}$ Average serum osmolarity: 275-295 mosmol/L

SEVERITY OF DKA

Grade	Arterial pH	Serum bicarbonate	Anion gap	Mental status
✓ Mild	> 7.24 – 7.30	15 – 18 mEq/L	> 10 mEq/L	Alert
✓ Moderate	7.0 – 7.24	10 – 15 mEq/L	> 12 mEq/L	Alert or drowsy
✓ Severe	< 7.0	< 10 mEq/L	> 12 mEq/L	Stuporous

TREATMENT OF DIABETIC KETOACIDOSIS (DKA)

Rx

1. **Airway:** Ensure patient is maintaining own airway, sit patient up to prevent acidosis
2. **Breathing:** Check SpO_2 & correct hypoxia with supplementary O_2 , watch for Kussmaul breathing, which may be present to compensate for metabolic acidosis.
3. **Circulation:**

- ☞ Maintain 2 Large bore intravenous line (18 or 20 gauge)
- ☞ Vitals Monitor: B.P, pulse rate, Respiratory rate, Temperature, SpO_2 x 4 hourly
- ☞ Monitor labs: Blood sugar level x 1 hourly, electrolytes level and ABGs every 4 hourly.
- ☞ **Insulin therapy: Pak. *Brands (Humulin-R/Actrapid/Insuget-R)**
 1. Inj Regular Insulin x 5-10 units x IV (0.14mg/kg) + 5-10 units x Subcutaneous (0.4mg/kg) x stat
 2. **Regular Insulin Infusion:** 60 units (0.1mg/kg/hour) of Regular insulin injection in 100ml 0.9% N/S is prepared in 100ml IV chamber x IV x 10 mic drops/minute, **should be start if $K^{++} > 3.5$**
 3. Not to start IV Insulin if K^{++} level is < 3.3 , Maintain serum potassium between 4-5 mEq/L.
 4. Continuous IV insulin infusion until the anion gap is normal
 5. Once anion Gap is normal then shift the Patient to Subcutaneous (S/C) insulin
- ☞ **Fluid replacement therapy:** Extracellular fluid loss is replaced by 0.9% N/S (isotonic solution), Intracellular fluid loss is replaced by Dextrose 5% OR 10%. **(Fluid of choice is 0.9% N/S or 0.45% N/S)**
 - ☞ 0.9% Normal saline (N/S) should be infused rapidly to provide 1L/hour over the first 1-2 hours.
 - Next 24-48 hours:** Adjust Intravenous fluid rate and composition according to CVP, urine output, blood glucose, and corrected sodium levels.
 - ☞ Than 1L of 0.9% N/S in 2 hours
 - ☞ Than 1L of 0.9% N/S in 4 hours
 - ☞ Than 1L of 0.9% N/S in 6 hours
 - ☞ Than 1L of 0.9% N/S in 8 hours.
- » Change to 5% dextrose to maintain blood glucose $< 200 - 250$ mg/dL ($< 13.9 - 16.7$ mmol/L)
This will prevent the development of hypoglycemia and also reduced the chances of cerebral edema.

MOST HOSPITAL WARD/ER PROTOCOL AS FOLLOW:

- 1) First 1 - 2L 0.9% N/S is given fast in 1 hour.
 - 2) Then 3rd drip of 1L 0.9% N/S is given at the rate of 125drops/minute.
Add 20ml (20-40mEq/L) of KCL to each Liter of 0.9% of N/S once K is < 5.5
 - 3) Then 4th drip of 1L 0.9% N/S + KCL 20ml is given at the rate of 88 drops/minute
 - 4) Then 5th drip of 1L 0.9% N/S + KCL 20ml is given at the rate of 33 drops/minute
 - 5) Then 6th drip of 1L 0.9% N/S + KCL 20ml is given at the rate of 22 drops/minute
 - ☞ **If $pH = 7.0$ or < 7.0 despite adequate IV fluid resuscitation:** administer IV Inj Sodium Bicarbonate x 2vial (50ml/cc) in 500ml 0.45% N/S x over 1 hours.
 - ☞ **Acidosis** usually resolves with fluids and insulin therapy, the use of bicarbonate is usually not necessary
Current study: Sodium Bicarbonate should be avoided → Oxford textbook of medicine
 - ☞ Start 5% Dextrose if RBS value is $< 200-250$ mg/dL at the rate 125ml IV/hour
 - ☞ If RBS value is > 250 mg/dL changed dextrose into 0.9% N/S
4. **Disability & Exposure (Secondary Survey)**
- » Consider early HDU/ICU Admission
 - » NPO status in patients with high anion gap metabolic acidosis on insulin infusion
 - » Pass Nasogastric tube and folly's catheter (Input/output record x 1-4 hourly)
 - » Monitor pupillary reflexes and GCS level
 - » Inj. Calcium gluconate in 100ml 0.9% N/S over 15minutes if indicated (SOS)
 - » **Antibiotics for associated infection:** Inj. Ceftriaxone 2g (Oxidil, Titan, Rocephin) in 100ml 0.9%
Or Inj. Moxifloxacin 400mg/250ml (Moxiget, Avelox) x IV x OD
 - » PPIs: Inj Omeprazole 40mg (Risek, Ruling) x IV x OD
 - » Give appropriate analgesic if pain and anti-emetic if nausea/vomiting

HYPEROSMOLAR HYPERGLYCEMIC STATE (HHS)

Name:	Age:	Sex:	Date:
Temperature:	B.P.:	Pulse:	Resp. Rate:

HHS also known as Hyper Osmolar Nonketotic Coma (HONK)

HHS is the diagnosis in patients with type 2 diabetes who have hyperglycemia and hyperosmolality!

Mortality rates can be as high as 50% in these patients.

CLINICAL PRESENTATION OF HHS:

- ✓ Insidious onset (over days or weeks) in contrast to DKA (Rapid onset <24hr)
- ✓ History of severe stress, illness, hospitalization and bed-ridden ignored patient (CVA/stroke, fracture)
- ✓ Classic features of DM: Polydipsia, Polyuria
- ✓ Severe dehydration → Sign of volume depletion (Dry mucous membranes, decreases skin turgor), hypotension, and shock.
- ✓ The absence of features of DKA: Vomiting, rapid deep breathing (Kussmaul Respirations), fruity breath odor
- ✓ **Hyperosmolality**
- ✓ Features of Hyperviscosity Syndrome:
 - » CNS features: ASOC, Lethargy, Drowsiness, Confusion, Coma, Convulsions and CVA.
 - » Eyes features: Blurring of vision
 - » Cardiovascular features: Angina, Myocardial infarction, Ischaemic heart disease (IHD)

DIAGNOSTIC APPROACH

- ✓ Check Blood sugar level (BSL): >600 mg/dL (> 33.3 mmol/L)
 - ✓ Elevated Serum BUN (Blood, urea, nitrogen) and serum creatinine level
 - ✓ Serum electrolytes: deranged
 - ✓ Check serum bicarbonate (HCO_3^-)
 - ✓ Check Anion gap = $(\text{Na}^+ + \text{K}^+) - (\text{Cl}^- + \text{HCO}_3^-)$ or $\text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-)$
 - » Normal value 10-12 mmol/L.
 - » The anion gap in HHS is normal or close to normal.
 - ✓ Urinalysis: Glucosuria and very minimal/absent ketone in urine
 - ✓ Check ABGs: Normal (pH >7.30), Acidosis in HHS is mainly a result of dehydration and compromised end-organ perfusion.
 - ✓ Serum Osmolality → Elevated > 320 mosm/kg (> 320 mmol/kg)
- Formula for Hyperosmolality** = $2(\text{Na} + \text{K}) + \frac{\text{BUN}}{28} + \frac{\text{BSL}}{18}$
- Average serum osmolality: 275-295 mosmol/L
- ✓ Diagnostic workup to evaluate the underlying cause: HbA1c, CBC, serum LDH, LFTs, serum amylase & serum lipase, serum procalcitonin, blood culture, urine culture.
 - ✓ Radiology if indicated: CT scan abdomen, Chest X-ray and ECG.

DIAGNOSTIC CRITERIA

- ✓ Hyperglycemia: Blood sugar level > 600 mg/dL (> 33.3 mmol/L)
 - ✓ Ketonuria: Very minimal/absent urine ketones
 - ✓ Serum Osmolality: > 320 mOsm/kg
 - ✓ No acidosis: Blood pH > 7.3
 - ✓ Serum bicarbonate: > 15 – 18 mmol/L
 - ✓ Normal anion gap: >14 mEq/L
 - ✓ Serum lactate: may have ↑ lactate
- Increase glucose-induced stupor/coma without ketonemia or acidosis**

DKA VS HHS

- ✓ DKA: hyperglycemia, high anion gap metabolic acidosis, ketonuria/ketonemia
- ✓ Hyperosmolar hyperglycemic state (HHS): Hyperglycemia, hyperosmolality, and dehydration without ketonuria, Also known as Hyperosmolar Non-ketotic coma (HONK)



TREATMENT OF HYPEROSMOLAR HYPERGLYCEMIC STATE (HHS)

Rx

- ☞ Stabilize patient using ABCD&E approach
- ☞ Establish 2 large-bore intravenous (IV) access
- ☞ Consider early HDU/ICU Admission
- ☞ NPO status in patients, Pass Nasogastric tube and foley's catheter
- ☞ Vitals Monitor: BP, PR, RR, Temperature, SpO₂ x 4hourly
- ☞ Monitor: Blood sugar x 1hourly, ABGs (SOS), Input/output record x 1-4hourly, electrolytes 2hourly
- ☞ FLUID REPLACEMENT THERAPY: Extracellular fluid loss is replaced by 0.9% N/S (isotonic solution), Intracellular fluid loss is replaced by Dextrose 5% or 10%.
- ☞ Cautions: Rapid correction of hyponatremia can lead to central pontine myelinolysis.
 - » **Begin normal saline (fluid of choice) infusion before insulin therapy is started**
 - » The Average fluid deficit in HHS is in the range of 20% to 25% of total body water, or 8 to 12 L. By using the patient's usual weight in kg, normal total body water and water deficit can be calculated. One half of the fluid deficits should be replaced over the initial 12 hours and the balance over the next 24 hours when possible.
 - » Begin fluid resuscitation with 0.9% N/S at a rate of 15 to 20 mL/kg/hour during the first hour, followed by rates from 4 to 14 mL/kg/hour.
 - » Limit the rate of volume repletion during the first 4 hours to <50 mL/kg of normal saline.
 - » Once hypotension, tachycardia, serum hyponatremia, and urinary output improve, 0.45% N/S can be used to replace the remaining free water deficit.
 - First hour 1 – 2L of 0.9% N/S, than 1L of 0.9% N/S over following 4 – 5 hour
 - Than 1L of 0.9% N/S in 2 hours, Than 1L of 0.9% N/S in 4 hours, than 6 hours, than 8 hours, than 12 hours. Add 20ml (20-40mEq/L) of KCL to each Liter of 0.9% of N/S once K is <3.5
- ☞ **Regular Insulin therapy (Humulin-R, Actrapid, Insuget-R)**

Less Insulin may be required to reduce the hyperglycemia in non-ketotic patients as compared to those with DKA coma. Bolus insulin is not needed. IV fluid replacement alone can sometimes precipitously decrease serum glucose level, so insulin dose may need to be reduced.

 1. Inj. Regular Insulin recommended dose is 0.1 – 0.14mg/kg x IV infusion
 - » Goal is glucose ↓ by 50 milligram/dL/h (2.8 mmol/L/hr).
 - » If glucose ↓ >70 milligram/dL/hr (>3.9 mmol/L/hr), decrease insulin to 0.05 units/kg/hr.
 - » If glucose ↓ <50 milligram/dL/hr (<2.8 mmol/L), increase insulin to 0.14–0.20 units/kg/hr.
 2. Insulin Infusion: Regular insulin 10-12 units (80 kg person) in 50ml 0.9% N/S is prepared in IV chamber x IV x 10 mic drops per minute
 3. Care should be taken to avoid starting insulin drip in the initial stage of treatment as this might cause a rapid drop in serum glucose levels leading to cerebral edema. It is recommended to try to keep the glucose level around 300 mg/dL to prevent the development of cerebral edema.
 4. Once the patient is mentally alert and able to eat and prior to discontinuing parenteral insulin
 5. Start 5% Dextrose if RBS value is <250-300 mg/dL at the rate 125ml IV/hour and reduce the insulin infusion to 0.02 to 0.05 unit/kg/h until serum osmolality is <315 mOsm/kg
 6. If RBS value is >300mg/dL changed dextrose into 0.9% N/S
- ☞ **Magnesium deficits** with 1 to 2 grams of magnesium given over 1 hour.
- ☞ **Potassium deficit:** If serum K⁺ is <3.3 mEq/L, give 40 mEq K⁺ until K⁺ ≥3.3 mEq/L
The serum potassium in HHS is usually high, but the total body potassium is low as a result of the extracellular shift from lack of insulin.

HYPOTHYROIDISM

Clinical Features

- General/Skin appearance: fatigue, dry, cool skin, brittle hair, diffuse alopecia, brittle nails, puffy facies and generalized non-pitting edema (myxedema)
- Metabolic: Cold intolerance, fatigue, decrease sweating, weight gain despite poor appetite, hyponatremia
- Nervous system: Depression, sluggish reflexes, paraesthesia, cerebellar ataxia.
- ENT: dysphagia, hoarseness of voice
- Cardiovascular: Bradycardia, dyspnea on exertion, hypertension (diastolic) and Myxedematous heart disease (dilated cardiomyopathy, bradycardia, dyspnea)
- Gastrointestinal: Hypo-defecation/ Constipation (decrease GI motility)
- Urogenital system: Decrease libido, delayed ejaculation, erectile dysfunction, menorrhagia, hyperprolactinemia, galactorrhea, Infertility
- Ocular (eye): Periorbital edema
- Musculoskeletal: Myalgia, Hypothyroid myopathy (proximal weakness, increase CK), carpal tunnel syndrome, myoedema (small lump rising on the surface of a muscle when struck with a hammer)
- Goiter (in Hashimoto thyroiditis) or atrophic thyroid (in atrophic thyroiditis)

Diagnostic workup

- Thyroid function tests (TFTs): (Free T3, Free T4 & TSH)
 - Send TSH level for all patients: ↑ TSH with classic clinical features is typically diagnostic for primary hypothyroidism (TSH is best initial screening test)
 - If TSH level is abnormal, send Free T4 (FT4).
 - FT4 (Decrease) is confirmatory test for primary hypothyroidism if TSH is raised.

Interpretation of TFTs in suspected hypothyroidism

Type	TSH	FT4	FT3
Subclinical hypothyroidism	↑	N	Normal(N)
Primary hypothyroidism	↑	↓	Normal/↓
Secondary hypothyroidism	↑	↓	Normal/↓
Tertiary hypothyroidism	↓	↓	Normal/↓

2. Antibody Testing

- Thyroglobulin Antibody (Tg-Ab) and Thyroid Peroxidase Antibody (TPO-Ab): Detectable in most patients with autoimmune hypothyroidism.
- TSH Receptor Antibody (TR-Ab): +ve in up to 20%

Autoimmune hypothyroidism ↑TSH, FT4↓ & TPO Antibodies +ve

- Radioactive iodine uptake test: Measures the proportion of exogenous iodine that is taken up by the thyroid (normally 10-35%). Decreased uptake indicates hypothyroidism.

- Ultrasound thyroid: Useful for the assessment of thyroid vascularity, goiters, and thyroid nodules

5. Baseline investigation for associated condition

- CBC: ↓Hb, ↓MCV (mild anemia) » Fasting lipid profile: ↑ LDL, hyperlipidemia
- Blood sugar level: ↓ (Hypoglycemia) » Creatine kinase: ↑ in hypothyroid myopathy
- Serum electrolytes: maybe abnormal (↓ sodium)

TREATMENT OF HYPOTHYROIDISM

- General Principles: Lifelong replacement, Prompt initiation
- Tab. Levothyroxine 50mcg or 75mcg or 100mcg (Thyronorm)
 - Dosage: 1.6 µg/kg body weight (typically 100-150 µg). Graves' disease, there is often underlying autonomous function, necessitating lower replacement doses (typically 75-125 µg/day).
 - Adult patients under 60 without evidence of heart disease may be started on 50-100 µg
 - Levothyroxine is a synthetic version of thyroxine
- OR Tab. Thyroxine 50mcg (Thyroxine sodium) x Twice daily (I - O - I)
 - Malabsorption can interfere with intestinal absorption of thyroxine, as can soy-containing foods and some medications (e.g., oral iron tablets, calcium carbonate, aluminum hydroxide, sucralfate, and cholestyramine)
 - As a result, thyroxine should be given 4 or more hours before or after such medications.

HYPERTHYROIDISM & THYROTOXICOSIS

CLINICAL FEATURES

- General/Skin appearance: weakness, fatigue, warm, moist skin, fine hair, onycholysis, Infiltrative dermopathy, especially in the pretibial area (pretibial myxedema)
- Metabolic: Heat intolerance, increase sweating, weight loss despite good appetite
- Nervous system: Hyperactivity, restlessness, anxiety, insomnia, depression, fine tremors, hyper-reflexia (brisk)
- Cardiovascular: Tachycardia, palpitations, dyspnea, irregular pulse (due to Atrial Fibrillation/Ectopic beats), chest pain and hypertension (systolic)
- Gastrointestinal: Hyper-defecation/diarrhea, Frequent bowel movements (increase gastro-intestinal motility)
- Urogenital system: Dec. libido, erectile dysfunction, menorrhagia, hyperprolactinemia, gynecomastia, infertility
- Ocular (eye): Ophthalmopathy in Graves' disease (including periorbital edema, exophthalmos), lid retraction (staring look)/lid lag (increase sympathetic stimulation of levator palpebrae superioris & superior tarsal muscle)
- Musculoskeletal: Thyrotoxic myopathy (proximal weakness, normal CK), osteoporosis/Increase fracture rate (T3 directly stimulates bone resorption)
- Goiter: Diffuse, smooth, nontender goiter; often audible bruit at the superior poles. Also seen in subacute thyroiditis, toxic adenoma, and toxic Multi nodular goiter

DIAGNOSTIC WORKUP

- THYROID FUNCTION TESTS: Initial screening test: TSH level – low/undetectable; a normal TSH level usually rules out hyperthyroidism.

INTERPRETATION OF THYROID FUNCTION TEST

- ↓ TSH, ↑ Free T4: Primary Thyrotoxicosis
- ↓ TSH, Normal Free T4 and total T3: Mild or subclinical thyrotoxicosis
- ↓ TSH, Normal Free T4, ↑ total T3: T3 thyrotoxicosis
- Normal or ↑ TSH, ↑ Free T4 and ↑ total T3: Thyrotropic adenoma (TSH-secreting pituitary adenoma)

BASELINE INVESTIGATION

- CBC: Leukocytosis and/or mild anemia
- LFTs: Mildly elevated AST, ALT, ALP and bilirubin
- Fasting lipid profile: ↓ total cholesterol, LDL, and HDL
- Blood sugar level: Hyperglycemia
- Serum calcium level: Mild hypercalcemia
- ESR: typically, ↑ (> 100 mm/hour) in subacute thyroiditis
- TSH Receptor Antibody (TRAb): if Graves' disease is suspected but classic clinical features are absent
- ECG: Tachycardia, Atrial fibrillation, LBBB and ECG signs of LVH in patients with dilated cardiomyopathy
- Nuclear medicine thyroid scan and Radioactive iodine uptake measurement: First-line test for most patients with uncertain etiology of thyrotoxicosis after initial evaluation
- Thyroid ultrasound with Doppler: Palpable abnormality, e.g., goiter or nodules
- Ultrasound-guided FNAC
- Chest PA and Lateral x-ray demonstrates thyroid enlargement due to goiter.

Rx

TREATMENT OF HYPERTHYROIDISM

1. Tab. Propranolol 40mg (Inderal, Cardinal)
 $\frac{1}{2}$ – $\frac{1}{2}$ – $\frac{1}{2}$ (Half tablet x TDS), than 1 – 1 – 1 (TDS)
 Dosage: started as 20 to 40mg every 8 hours and then titrated every three days to a maximal daily dose of 240mg as needed to control symptoms
2. Tab. Carbimazole 5mg (Neomercazole)
 $2 - 2 - 2$, (2 tablets x TDS) $3 - 3 - 3$, (3 x TDS) $4 - 4 - 4$ (4 x TDS)
 » Initial dose: 30–60 mg orally/day x TDS per oral until normal function, than start maintenance therapy.
 » Lower dose of 10–20 mg/day for very mild symptoms
 » Maintenance dose: 5 to 15mg/day x once or twice daily
 » Duration of therapy: 12 – 18 months. The starting dose of antithyroid drugs can be gradually reduced (titration regimen) as thyrotoxicosis improves.
 OR Tab. Propylthiouracil (PTU) 50mg (Procarbazole)
 » Dosage: 100–200mg per day in 3 – 4 divided doses

PHEOCHROMOCYTOMA

Definition: Pheochromocytoma is a tumor arising from catecholamine-producing chromaffin cells of the adrenal medulla that is characterized by classical features due to excess sympathetic nervous system stimulation and involve episodic blood pressure crises with paroxysmal headaches, diaphoresis, palpitations, and pallor. However, pheochromocytomas may also be asymptomatic or manifest with persistent hypertension.

- » Most common tumor of the adrenal medulla in adults
- » Pheochromocytoma are usually benign (~ 90% %) but may also be malignant.
- » Common in age: 3rd – 5th decades of life.

Risk factors:

- » Multiple endocrine neoplasia (MEN) syndrome type 2A and 2B
- » Von Hippel-Lindau (VHL) disease
- » Succinate dehydrogenase (SDH) subunit-B, -C, and -D genes mutations
- » Neurofibromatosis type-1 (NF-1)

Complications include hypertensive crisis, myocardial infarction, and hypotension.

CLINICAL FEATURES

Clinical presentation is related to fluctuating levels of excess epinephrine, norepinephrine, and dopamine secretion, therefore, symptoms are relapsing and remitting (episodic hyperadrenergic syndrome).

- » **Episodic hypertension** (or persistent hypertension in some cases) → Triggers for paroxysmal elevations in blood pressure – foods and beverages high in tyramine; (e.g., red wine, aged cheese), surgery, pressure on the tumor (e.g., during massage), or certain drugs (Beta blockers, MAOIs)
- » **Paroxysmal**
 - Throbbing headache
 - Diaphoresis
 - Palpitations, tachycardia
 - Pallor
 - Abdominal pain and nausea
 - Anxiety
- » Weight loss due to increased basal metabolism
- » Hyperglycemia
- » Signs of polycythemia, if Erythropoietin (EPO) is secreted
- » **Other features consistent with associated familial disorders:**
 - **MEN 2A:** Medullary thyroid cancer, pheochromocytoma, and parathyroid hyperplasia
 - **MEN 2B:** Medullary thyroid cancer, pheochromocytoma, oral/intestinal neuromas, & marfanoid habitus
 - **Neurofibromatosis type-1 (NF1):** Cutaneous neurofibromas, cafe-au-lait spots, and Lisch nodules
 - **Von Hippel-Lindau syndrome (VHL):** Renal cell carcinoma, hemangioblastoma, angiomatosis, and pheochromocytoma

DIAGNOSTIC WORKUP

Whenever possible, all medications should be put on hold one week prior to testing.

- » **Best initial test:** Plasma fractionated free metanephrines test (Most sensitive test)
- » **Confirmatory test:** urine metanephrines and creatinine in 24-hour urine (high specificity)
- » **Plasma fractionated catecholamines:** may be helpful to confirm whether an adrenal tumor is secretory pheochromocytoma.
- » **Clonidine suppression test** (rarely used) – can help distinguish whether elevated plasma free normetanephrine levels are physiologic or indicative of pheochromocytoma.
- » **Genetic testing:** if MEN2A, MEN2B, NF1, or VHL is suspected
- » **Immunohistochemical staining:** Positive for chromogranin, synaptophysin, and NSE
- » **Other diagnostic tests.**
 - 24-hour ambulatory blood pressure monitoring
 - **CBC** (erythrocytosis), **serum calcium** (may reveal hypercalcemia), **serum potassium** (may reveal hypokalemia)
 - **Chromogranin-A:** Elevated in patients with pheochromocytomas and multiple other neuroendocrine tumors
 - **CT scan or MRI** Adrenal or abdominal and pelvis (after positive biochemistry tests to localize tumor)
 - **I-123 Meta-iodobenzylguanidine (MIBG) Scintigraphy**

TREATMENT OF PHEOCHROMOCYTOMA

Operable Disease: Management consists of preoperative blood pressure management and then surgery.

Medical treatment (Preoperative blood pressure management)

Patient WITHOUT hypertensive crisis

» Combined alpha-adrenergic & beta-adrenergic blockade with adjunct CCB

1. Alpha blockade

» First line: Tab. Phenoxybenzamine 10mg at dose 10 mg per orally twice daily, increasing gradually by about 10 mg per day about every 2-3 days until hypertension controlled.

Maintenance doses: 10mg to 120mg/day up to maximum dose 240 mg/day

» Second line: Tab. Doxazosin 2 mg or 4 mg (Cardura) at dose 2 – 4 mg orally once daily for 1-2 weeks initially, increase according to response, maximum 16 mg/day

2. Beta blockers after alpha blockade: Starting beta-blockers before alpha-blockers is contraindicated. Beta blockers cancel out the vasodilatory effect of peripheral beta-2 adrenoceptors, potentially leading to unopposed alpha-adrenoceptor stimulation, causing vasoconstriction and ultimately hypertensive crisis. Beta blockers is initiated after 3-4 days, if the average heart rate is greater than 80 beats/min. BP should be controlled before cardioselective beta-blockers are added for control of tachyarrhythmias.

» Tab. Atenolol 25mg OR 50mg OR 100mg (Tenormin, Normitab) at dose 25-100 mg orally once daily

» OR Tab. Metoprolol titrated 100mg (Merol, Mepressor) at dose 50 mg orally (immediate-release) twice daily initially, increase according to response, maximum 400 mg/day

3. Adjunct: CCBs are usually added to alpha-blockers, but may be used alone).

» Tab. Nifedipine 10mg (Adalat, Nifedil) Initially at dose 10-20mg three times daily

» OR Tab. Amlodipine 5mg (Norvasc, Sofvasc) at dose 5-10 mg orally once daily

CCBs are superior to Phenoxybenzamine for long-term use, since they cause less fatigue, nasal congestion, and orthostatic hypotension. Nifedipine and amlodipine are the most commonly recommended calcium-channel blockers in the setting of perioperative pheochromocytoma BP control. However, CCBs should not be used for patients with severe heart failure.

4. Hydration and high salt diet (> 5g per day): All patients should be volume expanded with isotonic saline. In surgical patients, postoperative hypotension may be avoided by adequate IV fluid replacement preoperatively. On the second or third day after alpha-adrenergic blockade, a high salt diet (>5 g per day) should be instituted to counteract catecholamine-induced volume contraction and orthostasis, which can be associated with alpha-adrenergic blockade. It is common practice to administer 2L 0.9% NS during the 24 hours before surgery.

Patient WITH hypertensive crisis

» Inj. Phentolamine at dose 5-20 mg intravenously as a single dose

» OR Inj. Nitroprusside at dose 0.3 to 0.5 micrograms/kg/min intravenous infusion initially, increase according to response, maximum 8-10 micrograms/kg/min

Surgical treatment:

» Benign: Procedure of choice is Laparoscopic tumor resection (Adrenalectomy), Open surgical resection is reserved for large or invasive tumors.

» Malignant: Surgical Debulking, Adjunct: Postsurgical chemotherapy, iobenguane I-131 or ablative therapy

Inoperable disease

» Non-surgical candidate with benign pheochromocytoma:

» Continue medical treatment with alpha blockade and beta blockers

» Adjunct: Iobenguane I-131 (also known as I-131 Metaiodobenzylguanidine [MIBG]) may be considered in symptomatic patients with an unresectable tumor if I-123 MIBG scintigraphy was positive

» Non-surgical candidate with malignant pheochromocytoma

» Continue medical treatment + Chemotherapy:

» Adjunct: Iobenguane I-131 (also known as I-131 Metaiodobenzylguanidine [MIBG] therapy) may be considered in symptomatic patients with an unresectable tumor if I-123 MIBG scintigraphy was positive

MIBG therapy: Because MIBG is similar in structure to norepinephrine, it is taken up by sympathetic nerve cells, including neuroblastoma or pheochromocytoma tumor cells, throughout the body. When MIBG is combined with radioactive iodine, it can be used as a treatment that delivers radiation directly to cancer cells.

» Otherwise, palliative treatment (chemotherapy, tumor embolization)

HYPERPROLACTINEMIA

ETIOLOGY

- » Prolactin-secreting pituitary adenomas (Prolactinomas)
- » Damage to the hypothalamus and/or infundibular stalk
- » Severe primary hypothyroidism:
 T₃/T₄ → ↑ TRH → ↑ prolactin
- » Certain types of focal epilepsy: directly after temporal lobe seizures, due to proximity to the hypothalamus
- » Chronic renal failure (CRF)
- » Stimulation of the reflex suckling arc in the chest wall (e.g., following chest wall surgery, post-herpes zoster)
- » Physiological causes: Stress, pregnancy, lactation, Nipple stimulation, crying baby, sexual orgasm, sleep and exercise

Drugs

- » Dopamine antagonists:
 - Antiemetics: metoclopramide, Domperidone
 - Antipsychotics: Haloperidol, Risperidone
- » MAO inhibitors, SSRIs & TCAs (Clomipramine)
- » Catecholamine depletors: Reserpine
- » Dopamine synthesis inhibitors: α-methyldopa
- » Oral contraceptive pills (OCPs)
- » Verapamil, estrogen and progestin
- » Amphetamines, opioids, nicotine & cocaine
- » H₂ Antagonists: cimetidine, ranitidine

CLINICAL FEATURES

Hormonal changes	Female	Male
↑ Prolactin	» Galactorrhea (in premenopausal)	» Galactorrhea is rare
↓ LH + ↓ FSH	» Primary and/or secondary amenorrhea, or irregular menses » Infertility	» Clinical features of ↓ Testosterone
↓ Testosterone	» Loss of libido	» Loss of libido, Erectile dysfunction, infertility » Gynecomastia, Reduced facial and body hair » Osteoporosis
↓ Estrogen	» Atrophic endometrium and vaginal atrophy (menopausal symptoms) » Osteoporosis (after several years)	» Little to no noticeable effects

DIAGNOSTIC WORKUP

- » Basal prolactin level: Blood sample should be collected at any time of day, with minimal venepuncture stress.
 - » Prolactinoma is the most likely cause if the prolactin blood level is permanently >200 ng/mL.
 - » Hypothyroidism and drug-induced hyperprolactinemia (with the exception of Risperidone) usually result in mild elevations of prolactin (< 100 ng/mL).
- » Prolactin stimulation test: a prolactinoma is the most likely diagnosis if the prolactin blood level does not increase
- » Serum TSH, Free T₄ levels: to exclude primary hypothyroidism
- » In premenopausal women: pregnancy test
- » MRI Brain with contrast: Able to detect small microadenomas, characteristic features of pituitary adenoma
- » Computerized visual field examination in patient with Macroadenoma may reveal U/L or bitemporal hemianopia



Rx

TREATMENT OF HYPERPROLACTINEMIA

- » Treatment with dopamine agonists
 - » Firstline: Tab. Cabergoline 0.5mg (Dostinex) at dose 0.25 mg orally twice weekly or 0.5 mg orally once weekly initially, increase by 0.5 mg/dose increments every 4 weeks, increase dose gradually until desired reduction in prolactin levels and/or tumor.
 - » Second line: Tab. Bromocriptine 2.5mg (Parlodel, Brotin) at dose 1.25 to 2.5 mg/day orally initially, increase by 2.5 mg/day increments every 2-7 days, increase dose gradually until desired reduction in prolactin levels and/or tumor.
 - » N.B. Women who experience nausea with oral preparations may find relief with deep vaginal insertion of cabergoline or bromocriptine tablets; vaginal irritation sometimes occurs.
- » Treat the underlying cause
 - » Transsphenoidal resection of the pituitary adenoma
 - » Sellar redaction therapy – rarely used, reserved for situations where medico-surgical therapy fails
 - » Medications known to increase prolactin should be stopped if possible.
 - » Women with microprolactinomas who have amenorrhea or are desirous of contraception may safely take estrogen replacement or oral contraceptives—there is minimal risk of stimulating enlargement of the microadenoma.
 - » Patients with infertility and hyperprolactinemia may be treated with a dopamine agonist to improve fertility.
- » Treatment of primary hypothyroidism: Tab. Levothyroxine (Thyronorm)

ACROMEGALY

- Definition: Acromegaly is a condition in which benign pituitary adenomas lead to an excess secretion of growth hormone (GH) and insulin-like growth factor 1 (IGF-1). In adults, whose epiphyseal plates are closed, if the condition occurs in children, before epiphyseal plate closure, it is known as gigantism
- Prevalence: 1 – 9/100,000 in the USA
- Age of onset: 3rd decade of life (mean age at diagnosis usually 40–45 years)
- Sex: female = male

ETIOLOGY

- Benign growth hormone-secreting pituitary adenoma (> 95% of cases)
- Very rare: Neuroendocrine or hypothalamic tumors, paraneoplastic syndromes

CLINICAL FEATURES

- Tumor mass effects
 - Headache, vision loss (bitemporal hemianopsia), cranial nerve palsies
 - Female: Oligomenorrhea, secondary amenorrhea, galactorrhea, vaginal atrophy
 - Male: Erectile dysfunction, decreased libido, decreased testicular volume
- Soft tissue effects
 - Doughy skin texture, hyperhidrosis
 - Deepening of the voice, macroglossia with fissures, obstructive sleep apnea
- Skeletal effects
 - Coarsening of facial features slowly progressing with age: enlarged nose, forehead, and jaw (macrognathia) with diastema (space or gap between two teeth)
 - Widened hands, fingers, and feet
 - Painful arthropathy (ankles, knees, hips, spine)

DIAGNOSTIC WORKUP

- Best initial single test: Serum IGF-1 concentration
 - Elevated IGF-1 level: acromegaly suspected; conduct oral glucose tolerance test (OGTT).
 - Normal IGF-1 level: acromegaly ruled out
- The most specific test: OGTT with baseline Growth hormone (GH) and measure GH after 2 hours
 - If GH suppressed: acromegaly ruled out
 - If GH not suppressed: confirmed acromegaly; conduct pituitary MRI to determine the source of excess GH Pituitary
- MRI brain – radiological investigation of choice
 - Usually shows a visible mass: confirmed GH-secreting pituitary adenoma
 - If normal: screen for an extra-pituitary cause (e.g., CT scan of the chest and abdomen, measure GHRH)



TREATMENT OF ACROMEGALY

- Treated with transsphenoidal adenomectomy.
- In patients with inoperable tumors or unsuccessful surgery, medication and radiotherapy are indicated to reduce tumor size and limit the effects of GH and IGF-1.
- Surgery
 - Procedure of choice for treating acromegaly: Transsphenoidal adenomectomy (preferred method)
 - Surgical debulking (in patients with parasellar disease and inoperable tumors)
- Medication
 - Somatostatin analogs: Octreotide, Lanreotide
 - Dopamine agonists: Cabergoline to reduce tumor size and GH secretion
 - GH receptor antagonists: Pegvisomant
- Radiotherapy
 - Conventional fractionated radiotherapy
 - Stereotactic radiosurgery (e.g., Gamma Knife, CyberKnife, proton beam)
- Follow-up
 - Assessing IGF-1 and random GH level 12 weeks after the surgery and then annually
 - Annual hormonal testing for hypopituitarism
 - Performing MRI at least 12 weeks after the surgery
 - Serial imaging with MRI in patients receiving pegvisomant

CUSHING'S SYNDROME (HYPERCORTISOLISM)

Definition: Cushing's syndrome is an endocrine disorder caused by excessive corticosteroids, most commonly due to exogenous corticosteroids administration (iatrogenic Cushing's syndrome). Cushing syndrome can also be caused by endogenous overproduction of cortisol.

- » **Primary hypercortisolism:** it is caused by autonomous overproduction of cortisol by the adrenal gland (e.g., due to an adrenal adenoma or carcinoma).
- » **Secondary hypercortisolism:** it is the result of elevated adrenocorticotrophic hormone (ACTH) due to overproduction by either a pituitary adenoma (Cushing disease) or ectopic, paraneoplastic foci (e.g., in patients with small cell lung cancer).

ETIOLOGY

1. **Exogenous (iatrogenic) Cushing syndrome:** Most common cause of hypercortisolism → Prolonged glucocorticoid (corticosteroids) therapy → hypercortisolism → decreased ACTH → bilateral adrenal atrophy
2. **Endogenous Cushing syndrome**

Overview table of endogenous Cushing's syndrome

Types	Primary hypercortisolism (ACTH-independent Cushing syndrome)	Secondary hypercortisolism	
		Pituitary ACTH production (Cushing disease)	Ectopic ACTH production
Frequency	5–10%	= 75%	= 15%
Sex	Female > male (4:1)	Female > male (4:1)	Female = male
Causes	Autonomous overproduction of cortisol by the adrenal gland → ACTH suppression → atrophy of the contralateral adrenal gland » Adrenal adenomas » Adrenal carcinoma » Macronodular adrenal hyperplasia	Pituitary adenomas → ACTH secretion → bilateral adrenal gland hyperplasia	» Paraneoplastic syndrome → ↑ACTH secretion → B/L adrenal gland hyperplasia » Carcinomas include: » Small cell lung cancer » Renal cell carcinoma » Pancreatic or bronchial carcinoid tumors » Pheochromocytoma » Medullary thyroid carcinoma

CLINICAL FEATURES

- » **Skin features**
 - » Thin, easy bruisability skin with ecchymoses
 - » **Stretch marks:** classically **purple striae** especially around the thighs, abdomen and breast.
 - » Hirsutism
 - » Acne
 - » If **secondary hypercortisolism:** often hyperpigmentation (darkening of the skin due to an overproduction of melanin), especially in areas that are not normally exposed to the sun (e.g., palm creases, oral cavity)
 - » Caused by excessive ACTH production because melanocyte-stimulating hormone (MSH) is cleaved from the same precursor as ACTH called proopiomelanocortin (POMC)
 - » Not a feature of primary hypercortisolism
 - » wound healing is impaired (delayed)
 - » Flushing of the face (Plethora)
- » **Neuro-psychiatric features**
 - » Anxiety, Sleep disturbance
 - » Irritability
 - » Lethargy, fatigue
 - » Memory deficits
 - » Depression
 - » Psychosis
- » **Musculoskeletal features:**
 - » Muscle atrophy causes weakness, with difficulty standing up from a seated position or climbing stairs.
 - » Patients may also experience backache, headache, Osteopenia, Osteoporosis, Pathological fractures, Avascular necrosis of the femoral head
- » **Endocrine and metabolic features**
 - » Insulin resistance → hyperglycemia → mild polyuria & thirst (with or without glycosuria)
 - » Dyslipidemia
 - » Most patient eventually develop central obesity (weight gain) with a plethoric "moon facies", buffalo hump and supraclavicular (dorsocervical) fat pad
 - » **Male:** Decreased libido
 - » **Female:** Decreased libido, virilization, and/or irregular menstrual cycles (oligomenorrhea)
- » **Other features**
 - » Secondary hypertension (= 90% of cases)
 - » Increased susceptibility to bacterial or fungal infections (due to immunosuppression)
 - » Peptic ulcer disease (PUD)
 - » Cataracts, glaucoma

DIAGNOSTIC APPROACH

- Routine laboratory tests: CBC, blood glucose, HBA1C, Fasting lipid profile, electrolytes, BUN, creatinine
- Not required to establish the diagnosis, but if performed, may show the following typical findings:
 - Serum electrolytes: Hyponatremia, hypokalemia (in cases of ectopic ACTH)
 - Blood glucose: $\uparrow\uparrow$ (Hyperglycemia) due to stimulation of gluconeogenic enzymes (e.g., glucose-6-phosphatase) and inhibition of glucose uptake in peripheral tissue.
 - Fasting lipid profile: Hyperlipidemia (hypercholesterolemia and hypertriglyceridemia)
 - CBC: Leukocytosis with relative granulocytosis (without left shift), eosinopenia and lymphopenia.

DIAGNOSTIC TESTS FOR HYPERCORTISOLISM

- Late-night (10–11 PM) salivary cortisol test:** Relatively high sensitivity & specificity for Cushing syndrome. A saliva sample is collected in tube at the patient's usual bedtime. (Normal < 4.0 nmol/L or < 150 ng/dL)
 - Supportive finding: $\uparrow$ salivary cortisol, consistently > 250 ng/dL (7.0 nmol/L) are considered abnormal.
- Overnight low-dose dexamethasone suppression test:** it is an easy screening test for hypercortisolism and is particularly sensitive for mild ACTH-independent hypercortisolism from an adrenal nodule.
 - Dexamethasone 1 mg is given orally between at 11 pm and serum collected for cortisol determination in the next morning between 8 and 9 am. (Normal < 1.8 mcg/dL or < 50 nmol/L)
 - Supportive finding: $\uparrow$ early morning serum cortisol level > 1.8 mcg/dL or > 50 nmol/L
- 24-hour urinary free cortisol and creatinine:** usually used to confirm hypercortisolism
 - Free cortisol is measured in a complete 24-hour urine collection.
 - Supportive finding: $\uparrow$ urine free cortisol (> 50 mcg/day or > 140 nmol/L) or free cortisol to creatinine ratio of greater than 95 mcg cortisol/g creatinine, helps confirm hypercortisolism.

DIAGNOSTIC TESTS FOR THE SOURCE (IDENTIFYING THE CAUSE) OF HYPERCORTISOLISM

- Initial evaluation**
 - Consider nonneoplastic and physiological causes of hypercortisolism based on clinical features and patient history (e.g., depression, heavy alcohol use, obesity) and in pregnant patients.
 - Obtain serum ACTH levels and DHEAS
 - Below 6 pg/mL or 1.3 pmol/L with a low serum DHEAS $\rightarrow$ suspect primary hypercortisolism (ACTH-independent) $\rightarrow$ adrenal tumors
 - Inappropriately normal OR elevated > 20 pg/mL $\rightarrow$ Suspect secondary hypercortisolism (ACTH-dependent) $\rightarrow$ pituitary or ectopic ACTH-secreting tumors.
 - Proceed based on the results.
 - If ACTH-independent hypercortisolism is suspected: Obtain adrenal MRI and/or adrenal CT scan.
 - Assess for an adrenal tumor: Adrenal adenoma, carcinoma, hyperplasia
 - The adrenal cortex contralateral to the tumor shows atrophy due to reduced ACTH stimulation.
 - If ACTH-dependent hypercortisolism is suspected: Obtain further testing.
- Further testing in patients with ACTH-dependent hypercortisolism:** The goal is to differentiate between Cushing disease and ectopic ACTH production. A combination of tests is often necessary.
 - Obtain MRI of the pituitary gland to evaluate for Cushing disease
 - May show Pituitary adenoma > 10 mm confirms Cushing disease.
 - If there is no evidence of a pituitary adenoma or findings are unclear, obtain either:
 - Bilateral sampling of the inferior petrosal sinus
 - Hormone testing in ACTH-dependent hypercortisolism
 - If ectopic ACTH production is suspected: imaging to locate the ACTH-producing primary malignancy: Small cell lung cancer (SCLC), Renal cell carcinoma (RCC), carcinoid tumors
 - Multiple studies are often necessary.
 - May include a thin-slice whole-body imaging (PET scan/CT scan) with ^{68}Ga -somatostatin receptor-PET/CT (^{68}Ga -DOTATATE-PET/CT) $\rightarrow$ most sensitive (82%) scanning technique
- Hormone testing in ACTH-dependent hypercortisolism**
 - CRH stimulation test and Desmopressin stimulation test: A combination of both tests is preferred to differentiate between Cushing disease and ectopic ACTH production.
 - Findings:
 - ACTH and cortisol levels increase further: Cushing disease is likely.
 - No increase in ACTH or cortisol levels: Ectopic ACTH production is likely.

DIFFERENTIAL DIAGNOSIS OF CUSHING SYNDROME

Lab Studies	Normal	Primary hypercortisolism	Ectopic ACTH secretion	Cushing disease
ACTH levels	↔	↓		↑
Low-dose dexamethasone suppression test	↓ cortisol		↔ cortisol	
High-dose dexamethasone suppression test	↓ cortisol	↔ cortisol		
CRH and Desmopressin stimulation tests	↑ ACTH, ↑ cortisol	↔ ACTH, ↔ cortisol		↑ ACTH ↑ cortisol

TREATMENT OF CUSHING SYNDROME (HYPERCORTISOLISM)



Treatment Approach

- To deliver high quality treatment to patient with Cushing's syndrome require a multidisciplinary team including a specialized surgeons and physician, endocrinologist, radiologists, cytologists, histopathologists and radiotherapists
- First-line treatment:** Curative surgery (surgical resection of the tumor). Radiotherapy and/or chemotherapy may be indicated as part of the management of the causative tumor.
- Surgical procedures**
 - Primary hypercortisolism: U/L or B/L laparoscopic or open adrenalectomy for adrenocortical tumors
 - Cushing disease: Transsphenoidal surgery treatment of choice
 - Ectopic ACTH production: Tumor resection with node dissection, as appropriate
- Second-line OR adjunctive therapy:** Pharmacotherapy with Enzyme inhibitors (ketoconazole, Metyrapone) suppress cortisol synthesis, while glucocorticoid antagonists (Mifepristone) block the action of cortisol in peripheral tissues.
 - Tab. Osilodrostat at dose 2mg orally twice daily initially, increase gradually according to response, max 60 mg/day
 - OR Tab. Ketoconazole (Nizoral, Spike) at dose 200mg orally three times daily initially, increase gradually according to response, maximum 1600 mg/day given in 2-4 divided doses.
 - OR Cap. Metyrapone (Metopirone) at dose 250mg to 1 g/day orally given in 3-4 divided doses initially, increase gradually according to response, maximum 6 g/day, maybe combined with ketoconazole
 - OR Inj. Pasireotide LAR (Signifor LAR) at dose 0.3 to 0.9mg subcutaneously twice daily; 10-40mg x IM every 28 day
 - OR Cap. Cabergoline 0.5mg (Dostinex) at dose 0.5mg-3.5mg PO twice weekly
 - OR Tab. Mifepristone at dose 300mg orally OD initially, increase gradually according to response, max 1.2g/day
 - OR Tab. Mitotane 500mg (Lysodren) at dose 3g - 5g per 24 hours
- Postsurgical corticosteroids replacement therapy:** Inj. Hydrocortisone 250mg/vial (Solu-cortif) at dose 10mg - 25 mg per kg/day orally given in 2-3 divided doses; usual dose is a larger dose in the morning (10-15 mg) and a smaller dose in the late afternoon (5-10 mg)
- Postsurgical pituitary hormone replacement therapy (HRT):**
 - Tab. Levothyroxine (Thyronorm) at dose 1.8 mcg/kg/day, per orally AND/OR
 - Testosterone transdermal at dose 2.5 to 7.5 mg once daily, titrate according to response in men
 - OR Inj. Testosterone cypionate 200mg/ml at dose 200mg x IM every 2 weeks, titrate according to response in men
 - OR Tab. Estradiol 2mg (Progynova) at dose 2 mg orally once daily in women
 - OR Tab. Estrogens, conjugated 0.625mg (Premarin) 0.625 to 1.25 mg orally once daily in women
 - AND Tab. Medroxyprogesterone 10mg (Provera) at dose 5-10 mg orally once daily on 10 days of each month if woman has intact uterus and on estradiol or estrogen

Surgical option: Bilateral adrenalectomy

- Indications of Bilateral adrenalectomy**
 - Primary hypercortisolism caused by bilateral adrenal disease (recommended curative treatment)
 - Emergency treatment in severe ACTH-dependent hypercortisolism that can't be controlled pharmacotherapy
 - Symptomatic treatment for metastatic or occult ectopic tumors
- Complication of bilateral adrenalectomy:** Nelson syndrome (post adrenalectomy syndrome)
 - Etiology:** Bilateral adrenalectomy in patients with a previously undetected pituitary adenoma
 - Pathophysiology:** Bilateral adrenalectomy → no endogenous cortisol production → no negative feedback from cortisol on the hypothalamus → ↑ CRH production → uncontrolled enlargement of preexisting but undetected ACTH-secreting pituitary adenoma → ↑ secretion of ACTH and MSH → manifestation of symptoms due to pituitary adenoma and ↑ MSH
 - Clinical features:** headache, bitemporal hemianopia (mass effect), cutaneous hyperpigmentation
 - Diagnostic investigation:** High levels of β-MSH and ACTH, Pituitary adenoma on MRI confirms the diagnosis.
 - Treatment:** Transsphenoidal surgical resection &/or pituitary radiotherapy (if the tumor can't be fully resected)





URINARY TRACT INFECTION (UTI)

Introduction: Urinary tract infections (UTIs) are infections of the bladder, urethra, ureters, or kidneys that are most commonly caused by bacteria, especially *Escherichia coli*. Infections of the bladder or urethra are called lower UTIs, whereas infections involving the kidneys or ureters are called upper UTIs. Because women have a shorter urethra and anal and genital regions that are closer in proximity, they are at higher risk of contracting UTIs than men.

Causative organisms: *E. coli* leading cause of UTI (approx. 80%), *Staphylococcus saprophyticus* is 2nd leading cause of UTI in sexually active women. *Klebsiella pneumoniae* is 3rd leading cause of UTI. *Proteus mirabilis* (Produces ammonia, giving the urine a pungent or irritating smell, & associated with struvite stone formation)

DIAGNOSTIC WORKUP

Best initial test for all patients: Urinalysis (Urine D/R)

Interpretation and finding of UTI on urinalysis/Urine D/R

- » **Pyuria** (presence of WBCs in the urine): **Positive** leukocyte esterase: an enzyme produced by WBC.
Findings: ≥ 5 WBC/HPF OR $\geq 8 - 10$ WBC/mm³.
- » **Bacteriuria** (presence of bacteria in the urine): **Positive** urinary nitrites: indicate bacteria that convert nitrates to nitrites (most commonly gram-negative bacteria, e.g., *E. coli*).
- » **Positive leukocyte esterase and/or nitrite**, but the presence of both strongly suggestive of UTI
- » **Other findings**
 - **Leukocyte casts** may indicate pyelonephritis.
 - **Hematuria:** microscopic or macroscopic hematuria may be present.
 - **Alkaline urine (pH > 8); and struvite crystals in sediment:** Indicates urease-producing organisms such as *proteus*, *klebsiella*, *staphylococcus saprophyticus*.
 - **Epithelial cells:** The presence of squamous epithelial cells can be a sign of contamination.
- » **Urine culture:** Significant bacteriuria defined as a value of $\geq 10^5$ CFU/mL [colony-forming units (CFU)/mL].
- » **Pregnancy test:** indicated in women of childbearing age.
- » **Ultrasound KUB:** rule out urinary tract obstruction.
- » **Plain X-ray KUB:** urinary tract stone, abscess.

CLINICAL FEATURES

- » **Dysuria:** a sensation of pain or discomfort during micturition (Burning micturition) $\pm$ **Fever**
- » **Urinary urgency:** a strong urge needs to void that may be accompanied by pain or a fear of urine leakage.
- » **Urinary frequency**
- » **Hematuria:** The presence of RBCs in urine.
- » **Suprapubic (abdominal) pain or tenderness**
 $\pm$ Costovertebral angle pain
- » **Features of BPH in men's:** pain in the prostatic/perineal area, hesitancy, nocturia, enlarged prostate, fever/rigors

INDICATION OF URINE CULTURE

- » Suspicion for complicated UTI or hospital-associated UTI
- » Suspicion for pyelonephritis or urosepsis
- » Suspicion for uncomplicated cystitis with either of the following:
 - History of recurrent UTIs
 - Equivocal urinalysis
 - Atypical symptoms
 - Concern for multiresistant pathogens, e.g., due to recent antibiotic use
 - Must in pregnant patients to determine sensitivity
 - Age ≥ 65 years
- » **Follow-up cultures for test of cure in the following cases:**
 - Non-resolving symptoms despite antibiotic treatment
 - Anatomic or functional abnormalities of the urinary tract
 - Continued pathological findings on urinalysis



Treatment of UTI (Firstline)

1. **Tab. Nitrofurantoin 100mg** x orally, BD for 5 days
OR **Tab. Sulfamethoxazole/trimethoprim (SMT/TMP)** (Septran DS, Bactrim forte) x orally, BD for 3 days
OR **Fosfomycin 3g sachet** (Focin, Monurol) x orally once
2. **Tab. Diclofenac Sodium 50mg** (Voren, Voltrel)
OR **Tab. Phenazopyridine 100mg** (Urilef, Uropin)
1-0-1 (BD) OR 1-1-1 (TDS)
3. **Syp. Sodium acid citrate** (Citralka, Alkacitron)
2-3 teaspoonfuls in a glass water x TDS
 $\pm$ **Cranberry Extract Sachets** (Cranmax Pro, Abocran)
One sachet in a glass water x twice daily (BD)



Treatment of UTI (second line)

1. **Tab. Co-Amoxiclav 625mg** (Augmentin, Calamox)
OR **Cap. Cefaclor 500mg** (Ceclor, Slate)
OR **Tab. Norfloxacin 400mg** (Noroxin, Utinor)
OR **Tab. Ciprofloxacin 500mg** (Novidate, Ciproxen)
1-0-1 x Twice daily (BD) orally for 5-7 days
2. **Tab. Diclofenac Sodium 50mg** (Voren, Voltrel)
OR **Tab. Phenazopyridine 100mg** (Urilef, Uropin)
1-0-1 (BD) OR 1-1-1 (TDS)
3. **Cranberry Extract Sachets** (Cranmax Pro, Abocran)
One sachet in a glass water x twice daily (BD)



ACUTE PYLONEPHRITIS

ETIOLOGY OF PYLONEPHRITIS

- » Pylonephritis usually caused by an ascending bacterial infection of the bladder (cystitis).
- » Less commonly due to hematogenous spread of infection to the kidney (for example – due to infective endocarditis)
- » **Organisms:**
 - » **Gram-negative bacteria:** *Escherichia coli* (= 75–90% of cases; leading cause), *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Proteus mirabilis*
 - » **Gram-positive bacteria:** *Enterococcus faecalis*, *Staph. Aureus* and *Staph. saprophyticus*
 - » **Candida infection:** esp. in immunocompromised patient
- » **Risk factors**
 - » Most common in women due to shorter urethras
 - » Pregnancy
 - » **Urinary tract obstruction**
 - **Foreign bodies:** indwelling urinary catheters or other urologic instrumentation
 - **Anatomical abnormalities:** benign prostatic hyperplasia (BPH), vesicoureteral reflux, nephrolithiasis, ureteral strictures.
 - » **Cystitis (bladder infection)**
 - » Recent administration of antibiotics (possible antibiotic resistance)
 - » Immunosuppression (HIV, diabetes mellitus)
 - » Acute kidney injury (AKI)

CLASSIFICATION OF PYLONEPHRITIS

The terminology used for classifying pyelonephritis is somewhat controversial and serves primarily to estimate the risk of atypical or antibiotic-resistant pathogens.

- » **Uncomplicated pyelonephritis:** Pyelonephritis in an immunocompetent, nonpregnant female with normal genitourinary anatomy and renal function
- » **Complicated pyelonephritis:** Pyelonephritis associated with any of the following risk factors for complications:
 - » Failure of outpatient therapy
 - » Sepsis
 - » Male sex
 - » Age > 60 years
 - » **Urinary tract pathology:** Obstruction, indwelling catheter
 - » Surgical history to the urinary tract or kidneys
 - » Hospital-acquired (nosocomial) infection
 - » Renal impairment
 - » History of nephrolithiasis
 - » **Immunosuppression &/or severe comorbidities:** e.g., diabetes mellitus, chronic corticosteroid use
 - » Pregnancy



CLINICAL FEATURES

- » Fever, chills
- » Flank pain
- » **Costovertebral angle tenderness:** Pain upon percussion of the flank (usually unilateral, may be bilateral)
- » **Dysuria** as well as other symptoms of cystitis (e.g., frequency, urgency)
- » Weakness
- » Nausea, vomiting
- » Diarrhea may also be present
- » Possible abdominal or pelvic pain

DIAGNOSTIC WORKUP

- » **Urinalysis**
 - » **Nonspecific findings of UTI**
 - **Pyuria:** Pus in urine (positive esterase on dipstick test)
 - **Leukocyturia:** WBCs > 5/hpf
 - **Bacteriuria:** Presence of bacteria in the urine
 - **Positive nitrites on dipstick test** indicates infection with a urea-splitting organism.
 - **Hematuria:** Macro or micro-hematuria
 - » **Other findings**
 - **WBC casts:** rarely, but strong indicator for pyelonephritis
 - **Urine pH of ≥ 7 :** associated with urea-splitting organisms.
 - **Epithelial cells > 5/hpf:** suggests contamination.
 - **Urine gram stain:** $>10^5$ CFU/mL suggests bacterial infection
- » **Urine culture with susceptibilities:** Perform in all patients with suspected pyelonephritis to determine the pathogen and any associated drug resistance.
- » **Blood cultures (2 sets):** Should be performed in all patients with suspected complicated pyelonephritis
- » **In young female:** Urine pregnancy test
- » **Additional blood tests**
 - **CBC:** Leukocytosis, & Left shift
 - **Inflammatory markers:** $\uparrow$ CRP & ESR
 - **Serum creatinine & BUN:** may be normal or elevated.

Radiological Investigation:

- » Radiological test is not routinely indicated in patients with suspected acute uncomplicated pyelonephritis.
- » Radiological tests serve to identify obstruction, abscess, or emphysematous pyelonephritis
- » **Consider in the following situations:** Complicated pyelonephritis, sepsis or septic shock, known or suspected nephrolithiasis, new decline in eGFR to <40 , recurrent pyelonephritis & no response to therapy within 2 days.
- 1. **Ultrasound KUB:** may show hydronephrosis from a stone or other source of obstruction
- 2. **CT abdomen with or without contrast:** may demonstrate decreased perfusion of the kidney or focal areas within the kidney and nonspecific perinephric fat stranding.
- 3. **MRI abdomen:** Pregnancy and Patients with contraindications to CT scan

UN-COMPLICATED PYELONEPHRITIS

- » Check urinalysis and order urine culture with susceptibilities (ideally before administering antibiotics).
- » Consider a single initial dose of empiric IV antibiotics:
 - » Inj. Ceftriaxone 1g (Oxidil, Rocephin, Titan) x diluted in 100 ml 0.9% NS x IV x once
 - OR Inj. Ciprofloxacin 400mg/100ml (Novidate DS, Ciplet DS) x IV x once
- » Encourage the patient to drink adequate amounts of fluids.
- » Consider hospital admission if there is concern for a complicated course.
- » Follow up on urine culture results and narrow antibiotic regimen accordingly.
- » **Start empiric oral antibiotic therapy:**
 1. Tab. Levofloxacin 750mg (Leflox) x Once daily (OD) = 0 – 0 – 1
 - OR Tab. Ciprofloxacin 500mg (Novidate, Ciproxen) x Twice daily (BD) = 1 – 0 – 1
- » **Consider analgesia pain/fever**
 2. Tab. Paracetamol 500mg (Panadol, Calpol, Febrol) x 1 – 2 tablets (500mg – 1000mg) x TDS
 - OR Tab. Diclofenac sodium 50mg (Voren, Voltral) x one tablet BD/TDS
 - OR Tab. Mefenamic acid 500mg (Ponstan forte, Mefnac DS) x 1 – 1 – 1 (TDS)
- » **Natural supplements which decrease the risk of UTIs and prevent recurrent UTIs**
 3. Cranberry Extract Sachets (Cranmax Pro, Abocran)
 - One sachet in a glass water x Twice daily (BD)
- » **Consider anti-emetic for patient with nausea/vomiting**
 4. Tab. Domperidone 10mg (Motilium, Domel) x 1 – 1 – 1 (TDS)
 - OR Syp. Motilium 1mg/ml (2 Teaspoonful three time daily)
 - کھانے سے 30 منٹ پہلے
- » **Duration of treatment:** 5 – 7 days

**Rx****Complicated Pyelonephritis (more detailed see ER Rx)**

- » Hospital admission
- » Maintain Intravenous access (IV cannula)
- » Obtain blood cultures (2 sets) and urine culture with susceptibilities (ideally before administering antibiotics).
- » **Start IV empiric antibiotic therapy for complicated pyelonephritis.**
 - » Inj. Ceftriaxone (Oxidil, Rocephin, Titan) 1 – 2g diluted in 100ml 0.9% NS x IV x OD
 - OR Inj. Ciprofloxacin 400mg/100ml (Novidate DS) x IV x BD
 - OR Inj. Ampicillin/sulbactam 1.5g (Ambac) x IV x TDS,
 - PLUS: Inj. Gentamicin 40mg/2ml (Genticin) at dose of 1mg/kg x TDS
- » **Establish source control:** Check to evaluate for an abscess and/or obstruction.
- » **Start IV fluid therapy**
- » **For analgesia/pain:** Inj. Paracetamol 1g/100ml (Provas, Paracet) x IV x STAT
- OR Inj. Ketorolac 30mg/ml (Toradol) dilute in 4-8ml 0.9% NS x IV STAT
- » **For nausea/vomiting:** Inj. Ondansetron 8mg/4ml x dilute in 100ml 0.9% NS x IV
- » **Identify and treat sepsis and any urinary tract obstruction.**
- » **Follow up on urine culture results and narrow antibiotic regimen accordingly.**
- » **Duration of treatment:** 10-14 days

NEPHROLITHIASIS (RENAL STONES)

- Definition:** Nephrolithiasis refers to the presence of crystalline stones (calculi) within the urinary system (kidneys and ureter). Such renal stones are composed of varying amounts of crystalloid and organic matrix.
- Ureteric stones (ureterolithiasis)** almost always originate in the kidney but then pass down into the ureter.
- Nephrolithiasis** is also known as kidney stones, renal stones, urolithiasis, or urinary calculi.
- Epidemiology:** Sex ratio (men > women), Peak incidence (45–70 years)
- Risk factors:** Personal or family history, Low fluid intake, dehydration, obesity, high protein intake, high salt intake, Loop diuretics (Frusemide) and other precipitants medications, Postcolectomy and/or postileostomy
- Clinical suspicion:** Consider nephrolithiasis (renal stones) in patients with unilateral (one sided) colicky flank abdominal pain ± radiating to back associated with nausea, vomiting, and/or hematuria. Patients are usually unable to sit still & move around frequently (opposed to patients with peritonitis, who usually prefer to lie still)

Overview – Classification of kidney stones

Stone type	Incidence	Etiology	Crystal appearance	Radiopacity	Prophylaxis
Calcium oxalate	≈75%	» Hypercalciuria » Hyperoxaluria » Hypocitraturia » ↓ Urine pH	Envelope or biconcave dumbbell-shaped crystals	Radiopaque	Urine alkalinization (because urine pH is acidic = pH ↓)
Uric acid	≈10%	» ↓ Urine pH » Hyperuricemia/Gout » Hyperuricosuria	Rhomboid or rosettes or needle shaped crystals	Radiolucent	Urine alkalinization
Struvite	≈5–10%	» UTI with urease-producing bacteria	"Coffin lid"-shaped crystals	Weakly Radiopaque	Urine acidification
Calcium phosphate	≈5%	» Hyperparathyroidism » Type-I Renal tubular acidosis (RTA-1)	Wedge-shaped prism crystals	Radiopaque	Urine acidification (because urine pH is alkaline = pH ↑)
Cysteine	<5%	» Cystinuria	Hexagonal-shaped	Weakly Radiopaque	Urine alkalinization

Clinical features

- » Sudden onset, acute, severe colicky flank pain
- » Pain Radiates anteriorly to the lower abdomen, groin, labia, testicles, or perineum
- » Nausea, vomiting
- » Hematuria, Dysuria, frequency, and urgency
- » Passage of gravel or a stone

Diagnostic workup

- » **CBC:** WBCs ↑ (Pyelonephritis, UTI)
- » **Serum BUN & serum creatinine:** ↑ level suggestive of acute kidney injury (AKI)
- » **Serum electrolyte:** may be normal
- » **Urinalysis (Urine D/R)**
 - ↳ Nonspecific findings of UTI (see UTI)
 - ↳ Nonspecific findings stones: hematuria (gross or microscopic) & Crystalluria
- » **Ultrasound KUB:** Obstructive uropathy due to stone blockage causes hydronephrosis, hydroureter, perinephric fluid)
- » **Non-contrast helical (spiral) CT abdomen:** Calculus size, location, density, and degree of obstruction, Hydronephrosis and/or hydroureter, Perinephric fat stranding
- » **Other:** serum uric acid, calcium, stone analysis, X-ray KUB, Intravenous pyelogram (IVP)
- » **In female:** Urine pregnancy test



TREATMENT OF RENAL STONE (CONSERVATIVE)

See emergency (ER) section for acute management

1. Adequate oral hydration: Increase oral fluid intake
2. Adjunct antibiotics indicated in case of concomitant UTI
 - ↳ Tab. Nitrofurantoin 100mg (Furilin, Furantin)
 - OR Tab. Co-Amoxiclav 625mg (Augmentin, Calamox)
 - OR Tab. Ciprofloxacin 500mg (Ciplet, Novidate)
 - 1–0–1 (BD)
3. Analgesia/pain management
 - ↳ Tab. Diclofenac sodium 50mg (Voren, Voltral)
 - OR Tab. Tramadol + Paracetamol (Distalgic, Tramal plus)
 - 1–0–1 (BD) OR 1–1–1 (TDS)
4. For spasm/colicky pain
 - ↳ Tab. Phenazopyridine 100mg (Urilef, Uropin) x BD/TDS
 - OR Tab. Drotaverine 80mg (Relispa forte, Nospa forte)
 - 1–0–1 (BD)

Expulsive therapy can reduce ureteral spasm and increase spontaneous passage rates by about 50%.

- ↳ Cap. Tamsulosin 0.4mg (Tamsolin, Manilow) x OD
- OR Cap. Silodosin 4mg (Silorap, Silat, Sildoso) x OD
- OR Tab. Terazosin 2mg or 5mg (Hytrin) x 2–5mg x BD/OD
- OR Tab. Doxazosin 2mg or 4mg (Cardura) x 2–4mg OD
- Note:** Silodosin is more effective than tamsulosin for promoting the passage of distal ureteral stones.

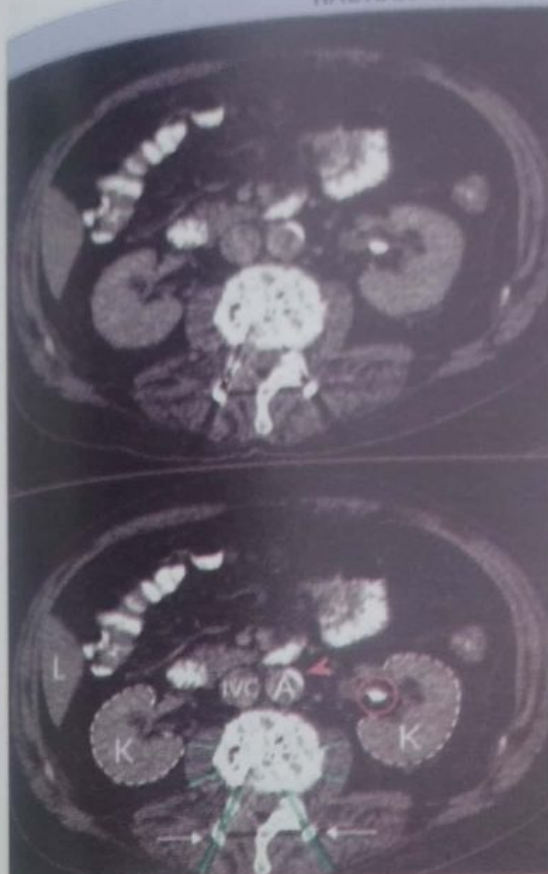


Fig. A. CT abdomen: Non-obstructive renal calculus 1/2

The calcific density (circled) in the left renal pelvis is a calculus. There is no dilatation of the renal pelvis to indicate obstruction. Atherosclerotic calcification (red arrowhead) of the abdominal aorta is seen. Metal streak artifacts (examples indicated in green) over the spine are caused by an internal spinal fixator (white arrows). A: aorta; IVC: inferior vena cava; K: kidney; L: liver



Fig. B. Excretory urography (AP view; left: pre-contrast; right: 2.5 hours post-contrast) shows obstructing ureteral calculus.

A calcification medial to the lower pole of the right kidney on the pre-contrast radiograph (red overlay) is shown post-contrast to be an obstructing proximal ureteral calculus (UC; red overlay). The right kidney is enlarged, with persistent enhancement (green overlay). There is pelvicaliectasis and poor contrast-filling of the right ureter (region indicated by dashed lines). The left renal collecting system is normal (green overlay). RP: renal pelvis; U: ureter; UB: urinary bladder

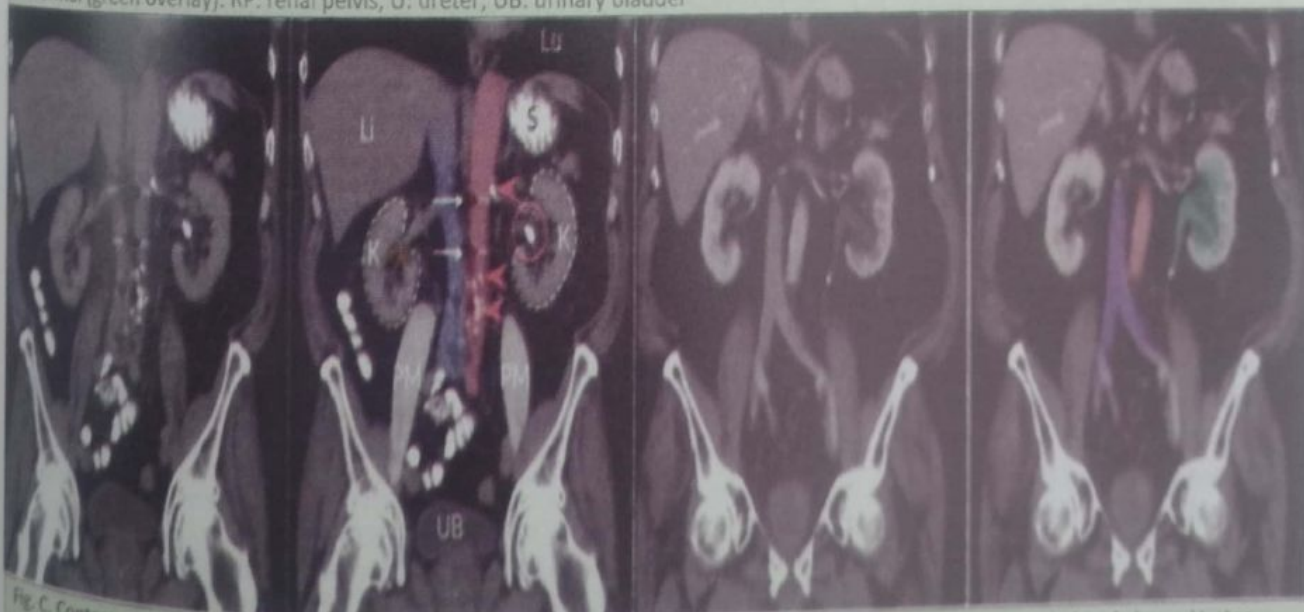


Fig. C. Contrast CT abdomen: Nonobstructive renal calculus (2/2)

A nonobstructive hyperdense calculus (red circle) is present in the left renal pelvis. Atherosclerotic calcifications (red arrowheads) of the abdominal aorta (red overlay) are also seen. Metal streak artifacts (blue overlay) between the aorta and IVC (blue overlay) are caused by an internal spinal fixator. K: kidney; L: liver; Lu: lung; PM: psoas major muscle; S: stomach with oral contrast; UB: urinary bladder

Fig. D. CT abdomen (with contrast; coronal plane) shows Ureter stone (Ureterolithiasis) with obstructive uropathy: The left renal collecting system (green overlay) is dilated to the level of a hyperdense calculus (yellow overlay) within the proximal third of the ureter. The left renal parenchyma shows less enhancement than the right renal parenchyma as a result of impaired excretion from ureteral obstruction. Blue overlay: IVC; red overlay: abdominal aorta

MEDICAL EXPULSIVE THERAPY (MET) – GUIDELINES

- Kidney stones 5mm or smaller have about a 70% probability of passing spontaneously, whereas stones between 5 & 7mm have a 60% chance, stones 7-9mm have a 48% chance, & stones 9mm or larger have a 25% chance of passing spontaneously.
- Stones located more distally in the ureter are more likely to pass spontaneously.
- Medical expulsive therapy (MET) may be cautiously attempted with ureteral stones < 10mm diameter for 4 to 6 weeks if pain is controlled, kidney function is normal, and there is no evidence of urinary tract infection or significant obstruction.
- The patient must be followed closely, generally with repeat ultrasound examinations every week or 2 weeks.

ONGOING MEDICAL THERAPY, DIETARY MODIFICATION & PREVENTION

- Oral alkalinization therapy with medications such as potassium citrate and sodium bicarbonate may be beneficial in dissolving uric acid stones and preventing uric acid supersaturation. It may be used for treating uric acid stones that do not require urgent surgical treatment, as well as asymptomatic stones. The ideal goal for alkalinization therapy for uric acid stones is to maintain the urine pH between 6.5 and 7.0. Potassium citrate is the first-line therapy. In patients with CHF or renal failure, extra care should be taken when prescribing alkalinization therapy. Alkalinization therapy also plays an important role in preventing calcium and cystine stones.
- Long-term dietary modification is essential for preventing future calculi: Increasing fluid intake (≥ 2.5 L/day). At least urine output 2L/day should be recommended to help prevent future episodes of stone formation. Decreased dietary sodium, protein, and oxalate should be recommended for stone prevention. Increased citrus fruit intake is recommended to prevent stone recurrence. Normal calcium intake (1000mg/day to 1200mg/day) is recommended. Dietary calcium restriction can lead to less binding of calcium to oxalate in the GI tract, promoting hyperoxaluria and potentiating the risk for stone formation; furthermore, it could have detrimental effects on bone health. Low calcium diets $\uparrow$ the risk of calcium-containing stone formation because they increase oxalate reabsorption! Reduced consumption of oxalate-rich foods and supplemental vitamin-C for oxalate stones.
- Depending on urinary pH and stone composition: urine alkalinization or acidification
- Where specific metabolic abnormalities exist and are not responsive to dietary modification, specific preventive therapies may be required. These include:
 - Uric acid stones: urinary alkalinization with potassium citrate or sodium bicarbonate
 - Hyperuricosuria (high urinary uric acid levels) with recurrent calcium oxalate stones, and normal urine calcium: allopurinol OR febuxostat (should only be prescribed for patients who can not tolerate allopurinol or where treatment with allopurinol has failed. An $\uparrow$ risk of death has been reported with febuxostat compared to allopurinol.
 - Hypercalciuria and recurrent calcium stones: thiazide diuretic with or without potassium supplementation (potassium citrate or potassium chloride)
 - Hypocitraturia and recurrent calcium stones: urinary alkalinization (e.g., potassium citrate; sodium bicarbonate or sodium citrate can be considered if the patient is at risk for hyperkalemia)
 - Hyperoxaluria: oxalate chelator (e.g., calcium, magnesium, or cholestyramine), potassium citrate, pyridoxine
 - Cystinuria: urinary alkalinization with potassium citrate, thiol binding agent (e.g., tiopronin which is tolerated better than D-penicillamine)
 - Struvite stones: urease inhibitor (e.g., acetohydroxamic acid), which is best reserved for complex/recurrent struvite stones in which surgical management has been exhausted. Secondary care supervision should be employed as it can produce severe adverse effects such as phlebitis and hypercoagulability.

Surgical Procedures/Urological interventions for renal stones (nephrolithiasis)

- Extracorporeal shock wave lithotripsy (ESWL):** Acoustic shockwaves used to fragment stones (noninvasive). Stones are localized using fluoroscopy or ultrasound.
Indication: ureteral stones, Lower renal pole stone ≤ 10 mm, All other renal stones ≤ 20 mm.
 - Ureterorenoscopy (URS):** Transurethral endoscopic visualization of the upper urinary tract with a rigid or flexible endoscope used for stone extraction and intraureteral lithotripsy (minimally invasive). Commonly combined with temporary ureteral stenting
Indication: ureteral stones, Lower renal pole stone ≤ 10 mm, All other renal stones ≤ 20 mm.
 - Percutaneous nephrolithotomy (PCNL):** Percutaneous insertion of a nephroscope into the renal pelvis under ultrasonographic &/or fluoroscopic guidance to remove stones (minimally invasive). can be combined with lithotripsy.
Indication: Lower renal pole stones > 10 mm, All other renal stones > 20 mm
 - Ureterolithotomy:** Open or laparoscopic stone removal. An incision is made into the ureter and the stone is removed. Rarely indicated. Reserved for patients for whom other interventions have been unsuccessful
- Prognosis:** Nephrolithiasis is a lifelong disease process. The rate of recurrence of nephrolithiasis is 50% at 5 years. The patients at highest risk for recurrence are frequently those who are not compliant with medical therapy and dietary/lifestyle modifications, or where underlying metabolic abnormalities exist.

BENIGN PROSTATIC HYPERPLASIA (BPH)

CLINICAL FEATURES

- Presence of Lower urinary tract symptoms (LUTS). Can be divided into obstructive and irritative symptoms.
- Obstructive symptoms include hesitancy, decreased force and caliber of the stream, sensation of incomplete bladder emptying, double voiding (urinating a second time within minutes), straining to urinate, prolonged postvoid dribbling & acute urinary retention.
 - Irritative symptoms include urinary urgency, dysuria, urinary frequency, and nocturia.
 - Additionally gross hematuria may be seen.
 - On physical Examination:
 - DRE (Digital rectal examination) usually results in a smooth (no nodules), firm, non-tender, rubbery, elastic enlargement of the prostate.
 - Examination of the lower abdomen should be performed to assess for a distended bladder.

DIAGNOSTIC WORKUP

- Urinalysis: to rule out UTI and hematuria. If UTI also obtained urine culture and sensitivity.
- Prostate specific antigen (PSA): Not routinely done. If Induration is noted on DRE, must alert the clinician to the possibility of cancer, & further testing with PSA should be done because it can detect asymptomatic prostate cancer.
- Interpretation of PSA level
 - Total PSA > 1.5 ng/mL: suggests an enlarged prostate (> 40 mL)
 - Total PSA > 4 ng/mL: increased likelihood of prostate cancer
- Serum creatinine is not routinely done as normal.
- Ultrasound KUB and Prostate with pre-void & post-void: Increased total prostate volume, Elevated post-void residual volume (>100ml), Evidence of bladder outlet obstruction (BOO) (e.g., bladder wall thickening, hydronephrosis)
- Transrectal USG (TRUS): indicated only if prostate cancer is suspected (e.g., abnormal DRE, elevated serum PSA)
- Uroflowmetry (Maximal urinary flow rate Measurement): normal maximal urinary flow rate > 15 mL/second
 - Maximal flow rates <15mL/second: bladder outlet obstruction
 - Maximal flow rates <10mL/second (due to BPH): indication for surgery
- CT pelvis or MRI pelvis (MRI for classification & differentiation)
- Cystometry: can indicate OAB

INTERNATIONAL PROSTATE SYMPTOM SCORE (IPSS)

The seven symptom questions constitute a scale initially developed by the American Urological association. The eighth question about quality of life is scored separately. (From Barry MJ, Fowler FJ Jr, O'Leary MP, et al. The American Urological association symptom index for benign prostatic hyperplasia: the Measurement committee of the American Urological association. J Urol. 1992; 148: 1549.)

QUESTIONARE	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always
1. Incomplete emptying: Over the past month or so, how often have you had a sensation of not emptying your bladder completely after you finished urinating?	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
2. Frequency: Over the past month or so, how often have you had to urinate again < 2 hours after you finished urinating?	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
3. Intermittency: Over the past month or so, how often have you found you stopped and started again several times when you urinated?	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
4. Urgency: Over the past month or so, how often have you found it difficult to postpone urination?	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
5. Weak stream: Over the past month or so, how often have you had a weak urinary stream?	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
6. Straining: Over the past month or so, how often have you had to push or strain to begin urination?	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
7. Nocturia: Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?	0 ☐ None	1 ☐ 1 time	2 ☐ 2 times	3 ☐ 3 times	4 ☐ 4 times	5 ☐ 5 times
8. Quality of life due to urinary symptoms: If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?						
Total IPSS Score = sum of questions 1-7 =						
Delighted	Pleased	Mostly satisfied.	Mixed—about equally satisfied & dissatisfied	Mostly dissatisfied	Unhappy	Terrible
0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐



- A scoring system based on the presence and severity of seven BPH symptoms in the past 30 days.
- International prostate symptom score (IPSS) also estimates the effect of LUTS on the quality of life.

Based on the final scores, BPH is graded as follows:

- 0–7 points: mild symptoms
- 8–19 points: moderate symptoms
- 20–35 points: severe symptoms

Rx

TREATMENT OF BENIGN PROSTATIC HYPERPLASIA (BPH)

- **Watchful waiting (Behavior modification):** Approximately 10% of symptomatic men may progress to urinary retention while 50% of patients improve spontaneously or even resolution of symptoms.
- **Lifestyle changes:**
 - » Restrict fluid intake before bedtime and going out.
 - » Avoid/reduce caffeine and alcohol intake.
 - » Education about bladder emptying techniques.
 - » Ensure emptying complete bladder, planned voiding.
- **Treatment for Lower urinary tract symptoms (LUTS) mainly due to Bladder outlet obstruction (BOO):**
 1. **Small prostate (< 40 mL) &/or serum PSA < 1.5 ng/mL: TREATED WITH Alpha blockers.**
 - » **Cap. Tamsulosin 0.4mg** (Tamsolin, Maxflow) x 0–0–1 (OD) at dose 0.4 mg, PO, once daily taken 30 minutes after a meal, taper as tolerated after 2–4 weeks (max. dose 0.8 mg/day)
 - » **OR Tab. Doxazosin 2mg OR 4mg** (Cardura) x started at a dose of 1mg per orally daily for 7 days, increased to 2mg daily for 7 days, then 4mg daily. Additional dose escalation to 8mg daily can be given if needed.
 - » **OR Tab. Terazosin 1mg OR 2mg OR 5mg** (Hytrin, Rozacin) x started at a dose 1 mg orally daily for 3 days, increased to 2 mg orally daily for 11 days, then 5 mg orally daily. An additional dose escalation to 10 mg orally daily can be performed if necessary.
 - » **OR Tab. Alfuzosin 5mg OR 10mg** (Xatral SR-5mg, Xatral LA-10mg) at dose 10 mg orally once daily with food, and it does not require titration.
 2. **Large prostate (> 40 mL) &/or serum PSA > 1.5 ng/mL: TREATED WITH 5-Alpha reductase inhibitors (5-ARIs)**
 - » Tab. Finasteride 5mg PO once daily
 - » Tab. Dutasteride 0.5 mg PO once daily
 3. **Severe symptoms or an inadequate response to monotherapy: TREATED WITH Combination therapy with alpha blocker AND 5-alpha reductase inhibitors (5-ARIs).**
 - » **Cap. Tamsulosin 0.4mg + Dutasteride 0.5mg** (Tamsolin Plus, Maxflow-D, Duodart)
 - » **OR Tab. Doxazosin 2mg OR 4mg** (Cardura) **PLUS** Tab. Finasteride 5mg PO once daily
- **Treatment for LUTS mainly due to Overactive Bladder (OAB): Antimuscarinic agent**
 - » Tolterodine 4 mg PO once daily
 - » **Tab. Darifenacin 15mg** (Deracin) at dose 7.5mg (Half tablet), per orally (PO), once daily; taper as tolerated every 2 weeks (max. dose 15 mg/day)
 - » **Tab. Solifenacin 5mg OR 10mg** (Solif, Solifen, Urgecin) at dose 5mg per orally (PO), once daily; taper as tolerated (max. dose 10 mg/day)
 - » **Tab. Oxybutynin 5mg** (Urobutin, Butyn, Cystrin) at dose 5–10 mg PO once daily (max. dose 30 mg/day)
- **Treatment for LUTS is caused by mixed BOO and OAB: An alpha blocker AND an antimuscarinic.**
- **Treatment for LUTS is associated with erectile dysfunction: Phosphodiesterase 5 inhibitor (Tadalafil).**
 - » **Tab. Tadalafil 5mg** (Cialis, Snafi, Tiafil, Procial) at dose 5mg once daily

SURGICAL MANAGEMENT

- **Gold standard treatment for surgical treatment of BPH: Transurethral resection of the prostate (TURP)—Over 95% of prostate surgeries can be performed endoscopically (through the urethra).**
- **Alternative surgical treatment options**
 - » **Large prostates (> 60g): Prostatectomy** (open, laparoscopic, or robotic) include: 1. **Suprapubic transvesical prostatectomy:** suprapubic enucleation of the prostate through the anterior wall of the bladder. 2. **Retropubic prostatectomy:** enucleation of the prostatic tissue through a retropubic transcapsular approach. 3. **Laser enucleation of the prostate (LEP):** Holmium laser enucleation of the prostate (HoLEP), Photovaporization of the prostate (PVP) and Thulium laser enucleation of the prostate (ThuLEP)
 - » **Average (31–60g) and small (≤ 30g) prostates:** radiofrequency-generated water thermotherapy, aquablation, prostatic urethral lift, transurethral vaporization of the prostate
 - » **Small prostates (≤ 30g): Transurethral incision of the prostate (TUIP) — more rapid and less morbid than TURP.**

URINARY INCONTINENCE

Definition: Urinary incontinence is defined as any involuntary leakage of urine. It may occur in patients with a normal urinary tract, as the result of dementia or poor mobility, or transiently during an acute illness or hospitalisation, especially more common in older individuals, and approximately twice as common in women than in men. [women's: mens (2:1)]. Stress incontinence and mixed incontinence are the most common types of incontinence in female patients. Urge incontinence is the most common type in male patients.

CLINICAL CLASSIFICATION OF THE DIFFERENT TYPES OF INCONTINENCE

1. **Stress incontinence:** involuntary leakage on effort, exertion, sneezing, or coughing
2. **Urge incontinence:** involuntary leakage accompanied by or immediately preceded by urgency
3. **Overactive bladder (detrusor overactivity):** urgency, usually with frequency, with or without urgency incontinence; usually with frequency and nocturia in the absence of an underlying metabolic or pathologic condition
4. **Mixed incontinence:** combination of stress and urgency incontinence symptoms
5. **Nocturia:** sleep interruption to urinate one or more times
6. **Nocturnal enuresis:** involuntary loss of urine occurring during sleep
7. **Continuous incontinence:** continuous loss of urine
8. **Overflow incontinence:** urinary leakage from an overdistended bladder; terminology is no longer widely used

ETIOLOGY

1. **Idiopathic**
2. **Neurological causes:** Multiple sclerosis, spinal injury, normal-pressure hydrocephalus, dementia, delirium
3. **Genitourinary causes:** Trauma to the pelvic floor, intrinsic sphincter deficiency, urethral hypermobility in women, impaired detrusor contractility, bladder outlet obstruction, pelvic floor weakness, urogenital fistula
4. **Transient causes of urinary incontinence:** Medications [Diuretics, anticholinergics, psychotropics, opioid analgesics, alpha-blockers (in women), alpha-agonists (in men), and calcium channel blockers (CCBs)], UTIs (Cystitis, pyelonephritis), postmenopausal atrophic urethritis, Psychiatric related (depression, delirium/confused state), Excessive urinary output (in disease like hyperglycemia, hypercalcemia, CHF), stool impaction, impaired mobility
5. **General risk factors:** Recurrent urinary tract infections (UTIs), obesity, caffeine, alcohol

EVALUATION FOR URINARY INCONTINENCE

Medical History:

- » Assess for onset, duration, and severity of symptoms.
- » Determine whether the incontinence is acute or chronic.
 - **Acute:** Screen for transient causes of urinary incontinence and reassess after they have been treated.
 - **Chronic:** Take a general history followed by a focused history.

General history

- » Review and screen for comorbid conditions/previous medical conditions and treatments
 - **Local causes:** back, bowel, gynecologic, or bladder surgery; constipation; pelvic organ prolapse
 - **Systemic conditions:** congestive heart failure, chronic cough, neurological disease, diabetes mellitus
- » Document medications that might affect bladder function (e.g., diuretics, anticholinergics).
- » Identify lifestyle factors (e.g., fluid intake, caffeine consumption).

Focused history of incontinence

- » **Questionnaires and Scales:** use a validated International Consultation on Incontinence Questionnaire.
- » Ask about symptoms that occur with voiding.
- » Assess for barriers to voiding (e.g., limited mobility, which may delay patients reaching the bathroom).
- » Ask patients to record fluid intake and micturition for 3–5 days using a voiding diary.

Physical examinations:

- » **General Examination:** Assess overall health and mobility. Evaluate cognitive function.
- » **Abdominal examination:** Check for bladder distention and masses. Perform a urinary stress test.
- » **Pelvic Examination (in women):** Evaluate for pelvic organ prolapse, vaginal atrophy, masses, and vaginitis.
- » **Digital rectal examination (DRE):** In men assess prostate size and consistency (prostatomegaly). Check for rectal masses, assess for fecal impaction and decreased anal sphincter tone.
- » **Cardiovascular examination:** Assess for signs of fluid overload (may worsen urge incontinence).
- » **Neurological examination:** Evaluate for signs of neurological impairment affecting bladder function.



DIAGNOSTIC WORKUP

- ☛ Detailed medical history and physical examination of the patients
- ☛ **Bladder (Voiding) Diary:** Record voiding patterns, fluid intake, and episodes of incontinence over several days.
- ☛ **Urinalysis:** If Positive for nitrites, WBCs suggestive of UTIs → send urine culture, if shows glycosuria → Diabetes, and RBCs suggestive with underlying infection or malignancy.
- ☛ **BUN & Creatinine:** To assess kidney function, may be elevated in patients with overflow incontinence
- ☛ **Ultrasound pelvis and renal ultrasound**
- ☛ **Post-void residual volume** – Determined by ultrasound or sterile catheterization. This is done after a spontaneous void. May confirm urinary retention. Results = elevated if ≥ 100 mL or $\geq 50\%$ voided volume.
- ☛ **Bladder stress test:** Routinely performed. The bladder is filled with 300 mL of sterile fluid and the patient performs a Valsalva maneuver while in dorsal lithotomy position. If leakage is observed, the test is positive. If not, look for cough leak on standing and with full bladder. If leakage is noted, the test is positive.
- ☛ **Pad test:** Used to quantify urine leakage over a 1–24-hour period. Patients are asked to wear a preweighed sanitary pad, perform certain activities, and drink a certain volume of liquid. The pad is then weighed again to measure urinary leakage.
- ☛ **Do urodynamic assessment or additional testing if indicated,** before any surgical intervention to exclude detrusor overactivity or sphincter dyssynergia.
 - » **Micturating cystourethrogram (MCU):** to detect morphological abnormalities
 - » **Urodynamic examination:** to measure bladder pressure and urethral closure pressure.
 - » **Cystoscopy:** to rule out tumors and vesicorectal or vesicovaginal fistulae
 - » **MRI:** to identify pelvic floor defects



CONSERVATIVE MANAGEMENT OF URINARY INCONTINENCE

Conservative treatment takes 6 to 8 weeks to obtain benefit, should be continue ideally for at least 3 months

- ☛ **Lifestyle modifications**
 - » **Weight loss:** recommended for overweight/obese patients
 - » **Diet modifications:** reducing intake of bladder irritants such as alcohol, caffeine, carbonated drinks
 - » **Smoking cessation**
 - » **Modification of other contributing factors such as drugs**
 - » **Fluid intake** should be regulated to 6 to 8 glasses or 30 cc/kg body weight per day with a 1500 mL/day minimum at designated times unless contraindicated by any illness.
- ☛ **Behavioral therapies and exercises**
 - » **Bladder training:** Scheduling bathroom visits/voiding and delayed urination, patient education are used to increase leak-free intervals.
 - ☞ **Timed voiding:** Intervals between voiding are sequentially increased until the goal of at least 3–4 hours is met.
 - ☞ **Relaxation and distraction techniques:** used to suppress the urge to urinate.
 - » **Pelvic floor muscle exercise (Kegel exercises):** regularly performed to strengthen pelvic floor muscles that control urinary flow and bowel movements.
- ☛ **Physical measures to prevent leakage**
 - » **Vaginal pessary** (a device inserted into the vagina in order to provide more support for pelvic organs) or penile compression devices
 - » Absorbent products
 - » Catheterization
 - » Urethral occlusion
- ☛ **Treatment of comorbidities may reduce symptom severity:** chronic cough, diabetes mellitus. Constipation
- ☛ **Review medication and, if possible, reduce the dose or discontinue contributing drugs** such as diuretics
- ☛ **Postmenopausal women with vaginal atrophy:** Topical vaginal estrogen

Rx
TREATMENT OF URGE URINARY INCONTINENCE/OVERACTIVE BLADDER (OAB)

- Monotherapy with Anti-muscarinic agents (First line):
 - » Tab. Solifenacin 5mg OR 10mg (Solif, Solifen, Urgecin) at dose 5-10mg orally once daily (OD)
 - » OR Tab. Fesoterodine 4mg OR 8mg (Toviaz) at dose 4-8mg orally once daily (OD)
 - » OR Tab. Tolterodine 2mg OR 4mg (Detrusitol, Detriflow) 2-4mg orally once daily (OD)
 - » OR Tab. Oxybutynin 5mg (Urobutin, Butyn, Cystrin) at dose 2.5-5mg orally two or three times daily
 - » OR Tab. Darifenacin 15mg (Dericin) at dose 7.5-15mg orally once daily (OD).
 - » OR Tab. Trospium chloride 20mg orally once or twice daily.
- ALTERNATIVE OR COMBINATION THERAPY
- With ONE above agent, PLUS ONE of the following:
 - » Tab. Mirabegron 25mg OR 50mg (Mirabet, Mibega) at dose 25-50mg orally once daily (OD)
 - » OR Cap. Tamsulosin 0.4mg (Tamsolin, Maxflow, Prostreat) x orally once daily (OD)
 - » OR Tab. Flavoxate 100mg (Uricon, Urivox, Genurin 200mg) at dose 100-200mg orally every 6 to 8 hours.
 - » OR if these treatments are ineffective, transdermal oxybutynin may be used: Oxybutynin transdermal patch, 3.9mg/day applied twice weekly; Oxybutynin 10% transdermal gel, 100mg applied daily.
- Notes: In men with both BPH and detrusor overactivity and with postvoid residual of 150 mL or less, an antimuscarinic agent added to an alpha-blocker may provide additional relief of lower urinary tract symptoms. Women who have persistent symptoms despite an adequate trial of initial treatment, or who are unable to tolerate pharmacotherapy options, may be referred to urologists or urogynecologists for alternative options
- Second-line treatment
 - » Endoscopic injection of botulinum toxin type A at different points in the bladder wall/detrusor muscle, Symptom relief from botulinum toxin injections has been reported to last 6-12 months; possible adverse effects include urinary retention and the need for self-catheterization.
 - » Neuromodulation: It can be delivered percutaneously to target the afferent input of the posterior tibial nerve, or via the sacral nerve stimulation directly.
 - » Bladder augmentation (also known as cystoplasty): it is a surgical alteration of the urinary bladder. It involves removing strips of tissue from the intestinal tract and adding this to the tissue of the bladder.

Rx
TREATMENT OF STRESS URINARY INCONTINENCE (URETHRAL INCOMPETENCE)

- Patient with urethral sphincter insufficiency: Duloxetine to enhance sphincter contraction
 - » Cap. Duloxetine 20mg at dose 40 mg orally twice daily
 - » OR Tab. Pseudoephedrine at dose 15-50 mg orally three times daily
- Antimuscarinic can be used, but they tend to only be effective in mild cases of stress incontinence.
- Patients with urethral hypermobility or displacement: surgery
 - » Indicated if conservative treatment does not provide sufficient improvement of symptoms
 - » Procedure of choice: midurethral sling to elevate the urethra. Alternative: urethropexy

Rx
TREATMENT OF OVERFLOW INCONTINENCE

- Most men with overflow incontinence from obstructive uropathy will first undergo bladder decompression with intermittent or indwelling catheterization followed by initiation of alpha-blocking agents (e.g., terazosin, 1-10 mg orally daily; prazosin, 1-5mg orally twice daily; or tamsulosin, 0.4-0.8mg orally daily taken 30 min after a meal).
- Finasteride, 5mg orally daily, can provide additional benefit in men with an enlarged prostate. If medical therapy fails to allow for adequate bladder emptying, surgical decompression can be an option. A variety of nonsurgical techniques make decompression feasible even for frail patients.
- For the nonoperative candidate with urinary retention, intermittent or indwelling catheterization are options.
- For the patient with a poorly contractile bladder, augmented voiding techniques (e.g., double voiding, suprapubic pressure) can prove effective. If further emptying is needed, consider intermittent or indwelling catheterization.
- Antibiotics indicated only for symptomatic UTI or as prophylaxis against recurrent symptomatic infections in a patient using intermittent catheterization; they should not be used as prophylaxis in a patient with an indwelling catheter.



MALE SEXUAL DYSFUNCTION & ERECTILE DYSFUNCTION

Definition: Erectile dysfunction can be defined as a man's inability to obtain rigidity sufficient to permit coitus of adequate duration to satisfy himself and his partner.

Epidemiology: Current estimates suggest that 10 to 15% of all American men suffer from erectile dysfunction, with the incidence progressively increased as men become older. Data from the Massachusetts Aging Study report that 52% of men 40 to 70 years of age experience some degree of erectile dysfunction. The prevalence of erectile dysfunction is even higher in men with type 2 diabetes mellitus and after radical prostatectomy for prostate cancer.

ETIOLOGY

Primary erectile dysfunction with normal functioning penis

» Psychogenic:

- Fear of intimacy, depression, stress, anxiety, or guilt
- Performance anxiety
- Common post-myocardial infarction secondary to anxiety

» ↓ Testosterone

» ↓ Libido

» ↓ Desire

» Thyroid disease

» Cushing's syndrome

Secondary erectile dysfunction with an abnormally functioning penis

- » **Vascular disease:** atherosclerosis causing decreases blood flow to the organ
- » Obesity
- » Diabetes mellitus
- » Hypertension
- » **Medications:** beta-blockers, antidepressants, and antipsychotics
- » Substance use, Alcohol
- » Penile disorders
- » **Neurologic:** stroke, seizures, multiple sclerosis
- » **Endocrine:** hypogonadism, hyperprolactinemia
- » Chronic prostatitis, prostate cancer, Peyronie disease
- » Pelvic trauma, surgery, or irradiation increase chances

Clinical features

Symptoms

- » Presence or absence of morning or nighttime erections → if present, this may suggest psychogenic etiology
- » Difficulty with arousal
- » Difficulty with orgasms

Physical Examination:

- » During the physical exam, vital signs, body habitus (obesity), and secondary sexual characteristics should be assessed.
- » Basic cardiovascular and neurologic examinations should be performed.
- » The genitalia should be examined, noting the stretched length of the penis, fibrosis of the penile shaft, and any abnormalities in size or consistency of either testicle.

» Erectile dysfunction should be distinguished from problems with penile deformity, libido, orgasm, ejaculation, and penile deformity.

» The severity, intermittency, and timing of erectile dysfunction should be noted.

Diagnostic workup (RACGP Guidelines)

- » Complete blood count (CBC)
- » Liver function test (LFTs)
- » Serum Electrolytes
- » Serum urea and creatinine
- » Fasting Lipid profile
- » Blood Glucose
- » Thyroid function test
- » Serum Testosterone level, Luteinizing hormone (LH) and progesterone level (hypogonadism)
- » Serum ferritin (Hemochromatosis may cause hypogonadism in Anglo-Celtic patients)

Rx

FIRST LINE TREATMENT

Alter modifiable risk factors

» Lifestyle changes

- » smoking and drug cessation
- » reduced alcohol
- » improved diet and exercise
- » stress reduction
- » Offending drugs such as estrogens, morphine, sedatives, and neuroleptics should be discontinued

» Compliance with diabetes and cardiovascular drugs

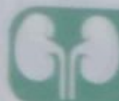
- » Modify medication regimen
- » Address psychosocial issues
- » Discuss sexual misinformation
- » Manage androgen deficiency: Give Testosterone

TREATMENT OF ERECTILE DYSFUNCTION (FIRST LINE)

- If patient has Irritative symptoms, low post-void residual volume and BPH
 - Cap. Tamsulosin 0.4mg (Tamsolin, Maxflow, Prostreat)
 - OR Tab. Solifenacin 5mg or 10mg (Solif, Solifen, Urgecin)
 - 0-0-1 (Once per orally daily)
- Patients with mild to moderate Erectile Dysfunction:
 - Tab. Sildenafil 50mg, or 100mg (Viagra)
 - » Dosage: initially starting dose of sildenafil is 50 mg, increasing in 25-mg increments up to 100 mg.
 - » Should be taken 25 to 60 minutes before intercourse. Duration of effect is approximately 4 hours
 - OR Tab. Vardenafil 10mg, or 20mg (Levitra)
 - » Dosage: initially starting dose of Vardenafil is 10mg, increasing in 10mg, Increments up to 20mg.
 - » Should be taken 20 to 60 minutes before intercourse. Vardenafil has a relatively longer duration of action (4 to 6 hours)
 - OR Tab. Tadalafil 5mg, or 10mg, or 20mg (Cialis)
 - » Dosage: initially starting dose of Tadalafil is 5mg, increasing in 10mg, Increments up to 20 mg.
 - » Should be taken 25 to 60 minutes before intercourse. Tadalafil has a faster onset of action and longer duration (36 hours)
 - OR Tab. Avanafil 50mg, 100mg, 200mg (Stendra)
 - » Dosage: initially starting dose of Avanafil is 100mg
 - » Maintenance dose: 50 to 200 mg orally as needed adjusted according to response to 50-200 mg
 - » Should be taken 25 to 60 minutes before intercourse. Avanafil has relatively longer duration (6 hours)
- Patients with severe Erectile Dysfunction without increasing side effects → Combination therapy
 - Long acting: Tab. Tadalafil (Cialis) at dose 2.5mg to 5mg
 - PLUS
 - Short acting: Tab. Sildenafil (Viagra) 50mg
 - » Should be taken 25 to 60 minutes before intercourse.

PRECAUTIONS

- Warn patients about potential side effects
 - » Color vision changes
 - » Headache, dyspepsia, facial flushing
 - » Sudden blindness from non-ischemic anterior optic neuropathy (case reports)
- Avoid in patients on nitrates (may induce hypotension) & those with recent or unstable coronary artery disease
- Fatty food Reduced absorption of Sildenafil, Vardenafil and Avanafil.
- All PDE-5 inhibitors are metabolized by cytochrome P450 isozyme 3A4 (CYP3A4); doses should be reduced when combined with inhibitors of CYP3A4 (erythromycin, ketoconazole, protease inhibitors, and grapefruit juice)



NEPHRITIC SYNDROME

Definition: Nephritic syndrome is characterized by glomerular capillary damage leading to hematuria, pyuria, water retention, and subsequent hypertension and edema.

ETIOLOGY

- Poststreptococcal glomerulonephritis (PSGN)
- IgA nephropathy (Berger disease)
- Eosinophilic granulomatosis with polyangiitis
- Microscopic polyangiitis
- Granulomatosis with polyangiitis
- Goodpasture syndrome (anti-GBM disease)
- Hereditary nephritis (Alport syndrome)
- Henoch-Schönlein Purpura nephritis

- Thin basement membrane disease
- Embolic nephritis
- Rapidly progressive glomerulonephritis (RPGN)
- Lupus nephritis
- Cryoglobulinemia
- Most common causes of nephritic-nephrotic syndrome
 - » Membranoproliferative glomerulonephritis (MPGN)
 - » Diffuse-proliferative glomerulonephritis (DPGN)

Clinical features

- » **Proteinuria:** < 3.5 g/day
- » Hematuria with acanthocytes (RBC casts in urine)
- » Mild to moderate edema
- » **Oliguria:** decreased urine output (little or no urine may be produced)
- » Hypertension
- » **Sterile pyuria:** WBCs or pus in the urine
- » **Azotemia:** increased serum urea & creatinine

Diagnostic workup

- » **Urinalysis:** nephritic sediment
 - » Hematuria (either microhematuria or intermittent macrohematuria)
 - » Acanthocytes
 - » **Red blood cell casts:** RBC casts form through the congregation of proteins and RBCs inside the tubules.
 - » Mild to moderate proteinuria of > 150 mg/24hr. but < 3.5 g/24hr. (nonselective glomerular proteinuria)
 - » Sterile pyuria & sometimes WBC casts
- » **Blood tests**
 - » Serum creatinine & BUN: ↑
 - » GFR: ↓
 - » Serum electrolytes
 - » Serum complement level;
 - ↳ Serum C3 level: Low in 90% cases
 - ↳ Serum C4 level: typically normal/low
 - » **Antibody tests:** ANA, ANCA, and anti-GBM antibodies test
 - » Blood culture
 - » **Evidence of recent throat infection:** Throat culture, ↑ ASO titers
 - » CBC: anemia
- » **Renal Ultrasound:** typically, normal.
- » **Renal biopsy** is providing definitive diagnosis.

Rx

- » **Water/fluid restriction** (<2L/day) to minimize the risk of edema (if not already present) or to reduce any active edema that may be present.
- » **Diet:** a special diet during the hospital stay that restricts sodium (<2g/day), potassium, and fluids in conjunction with the previously mentioned fluid restriction in an attempt to control symptoms of fluid overload.
- » **Treatment of underlying etiology**
- » **Monitor and correct electrolyte abnormalities** (hyperkalemia, hypocalcemia, hyponatremia and metabolic acidosis seen in severe cases)
- » **For proteinuria and/or hypertension:** ACEIs or ARBs
- » **For severe hypertension and/or edema:** Diuretics
- » **Steroids/NSAIDs:** to reduce active inflammation in the kidney.
- » **Antibiotics therapy:** Evidence of active GAS infection to prevent complications
- » Sometimes immunosuppressive therapy is indicated (e.g., in lupus nephritis).
- » **For RPGN from Anti-GBM antibody disease:** Plasmapheresis
- » **In the case of:**
 - » **Severe Renal Insufficiency OR Kidney Failure:** Renal replacement therapy (e.g., Hemodialysis, possibly transplantation)
 - » **Membranoproliferative Glomerulonephritis (type 1 and type 2 MPGN)**
 - ↳ RAAS inhibitors are often added to treatment
 - ↳ Prednisone alone OR in combination with other immunosuppressants (Cyclosporine OR Tacrolimus)

NEPHROTIC SYNDROME

DIAGNOSTICS WORKUP

Initial Evaluation	Additional Investigations
Confirmation of nephrotic-range proteinuria - Qualitative assessment by urine dipstick (commonly used for screening) - Usually shows $\geq 3+$ proteins - Hematuria may indicate concomitant glomerulonephritis. - Quantitative assessment of urine protein excretion 24-hour urine protein (test of choice): > 3.5 g/24 hours - Spot urine protein/creatinine ratio: > 3.5 g/g Urine sediment microscopy - Nephrotic sediment - Lipiduria, fatty casts with Maltese cross appearance under polarized light - Renal tubular epithelial cell casts - Hematuria with acanthocytes and/or RBC casts may indicate concomitant glomerulonephritis	- CBC: $\uparrow$ Hb/Hct may indicate hemoconcentration - Serum Creatinine, BUN & electrolytes: $\uparrow$ Cr and/or $\uparrow$ BUN may be seen; $\downarrow$ Na - Serum protein: $\downarrow$ total protein - Albumin: $\downarrow$ albumin (< 3 g/dL) - Coagulation factors: $\downarrow$ ATIII, $\downarrow$ protein S, $\downarrow$ Plasminogen; $\uparrow$ fibrinogen, $\uparrow$ D-dimer. - Fasting Lipid profile: Hyperlipidemia ($\uparrow$ LDL, $\uparrow$ triglycerides) may be present. - Vitamin D levels: $\downarrow$ 25-OH Vitamin-D - Inflammatory markers: $\uparrow$ ESR, $\uparrow$ CRP may suggest underlying infection, inflammatory condition, or vasculitis. - Blood glucose & HBA1C: to rule out DM - Antinuclear antibody test for collagen vascular disease, and a serum complement level, which screens for many immune complex-mediated diseases. - Renal ultrasound: to assess kidney size and shape and rule out obstruction

Clinical features

Classic manifestations

- Massive proteinuria > 3.5 g/24 hours
- Edema
 - Typically starts with periorbital edema
 - Peripheral edema (pitting)
 - Pleural effusion
 - Pericardial effusion
 - Ascites
 - In severe cases, anasarca
- Hypoalbuminemia
- Hyperlipidemia

Other clinical features

- Hypercoagulable state with increased risk of thrombosis and embolic events (e.g., pulmonary embolism, renal vein thrombosis)
- Increased susceptibility to infection
- Hypertension in some cases
- Possibly frothy urine
- Symptoms of hypocalcemia (e.g., tetany, paresthesia, muscle spasms)
- Symptoms of the underlying disease (e.g., malar rash in lupus nephritis)



- Treatment varies by the specific cause.
- Chronic oral anticoagulation with warfarin is needed if thrombotic complications occur and is commonly recommended in patients with additional risk factors for thrombosis (e.g., a prior idiopathic thromboembolic event, immobilization, severe heart failure, or morbid obesity).
- Warfarin also may be considered in patients who have membranous nephropathy with hypoalbuminemia (< 2.8 g/L) and who are at low risk for bleeding.
- Insufficient data exist with regard to the direct-acting oral anticoagulants.
- Edema is treated with a low-salt diet and loop diuretics.
- ACE inhibitors or ARBs often use to reduces proteinuria, increases the serum albumin level, and ameliorates the edema and hyperlipidemia.
- The combination of Loop diuretics (Furosemide) with Albumin may be effective in patients with severe edema and signs of volume depletion
- Treatment of Elevated lipid level (Hyperlipidemia)



ACUTE KIDNEY INJURY (AKI)

ETIOLOGY OF AKI

PRE-RENAL ACUTE KIDNEY INJURY

Prerenal causes include any condition that leads to decreased renal perfusion (=60% of cases of AKI).

- » **Hypovolemia:** e.g., due to hemorrhage, vomiting, diarrhea, burns, sweating, diuretics, poor oral intake, dehydration, hypercalcemia
- » **Hypotension:** e.g., due to sepsis, cardiogenic shock (decreased cardiac output), anaphylactic shock
- » **Decreased circulating volume (↓ effective arterial volume)**
 - » **Cardiorenal syndrome:** e.g., in congestive heart failure
 - » **Hepatorenal syndrome:** e.g., in cirrhosis, liver failure
 - » Abdominal compartment syndrome
 - » Nephrotic syndrome
 - » Acute pancreatitis
- » **Renal artery stenosis**
- » **Drugs that affect glomerular perfusion:** e.g., cyclosporine, tacrolimus, NSAIDs, ACE inhibitors (ACEIs)

POST-RENAL ACUTE KIDNEY INJURY

- » Postrenal causes include any condition that results in bilateral obstruction of urinary flow from the renal pelvis to the urethra (=5% of cases of AKI).
 - Acquired obstructions
 - Benign prostatic hyperplasia (BPH)
 - **Iatrogenic:** e.g., catheter-associated injuries
 - **Tumors:** bladder, prostate, cervical, metastases
 - Kidney stones
 - Bleeding with subsequent blood clot formation
- » **Neurogenic bladder:** e.g., due to
 - Multiple sclerosis
 - Spinal cord lesions, or
 - Peripheral neuropathy
- » **Congenital malformations:** e.g. posterior urethral valves

INTRINSIC ACUTE KIDNEY INJURY

Intrinsic causes include any condition that leads to severe direct kidney damage (=35% of cases of AKI).

- » **Acute tubular necrosis (causes =85% of intrinsic AKIs)**
 - » **Ischemia:** e.g., due to prolonged hypotension
 - » **Nephrotoxic drugs:** e.g., radiographic contrast agents, aminoglycosides, Cisplatin, methotrexate, ethylene glycol, amphotericin B
 - » **Endogenous toxins:** e.g., hemoglobin in intravascular hemolysis, myoglobin in rhabdomyolysis, uric acid in TLS, Bence-jones protein light chains in multiple myeloma
- » **Acute interstitial nephritis**
 - » **Medication:** e.g., antibiotics, phenytoin, interferon, PPIs, NSAIDs, cyclosporine
 - » **Infection**
 - **Bacterial:** e.g., Legionella spp., Streptococcus spp.
 - **Fungi:** Candida, Histoplasma
 - **Viral:** e.g., hepatitis C virus, cytomegalovirus, HIV
 - » **Infiltrative diseases:** e.g., sarcoidosis, amyloidosis
- » **Vascular diseases**
 - » Hemolytic uremic syndrome (HUS)
 - » Thrombotic thrombocytopenic purpura (TTP)
 - » Hypertensive emergency
 - » Vasculitis, scleroderma renal crisis
 - » Renal vein thromboses, renal atheroemboli, renal infarction
- » **Glomerulonephritis (Rapidly progressive glomerulonephritis)**

OVERVIEW OF NEPHROTOXIC MEDICATIONS

- » **Antibiotics:**
 - » Aminoglycosides
 - » Vancomycin
 - » Cephalosporins
 - » Colistin
 - » Sulfonamides
 - » Streptomycin
- » **Antivirals:**
 - » Acyclovir
 - » Foscarnet
 - » Cidofovir
 - » Tenofovir
 - » Interferon
- » **Antifungals:** Amphotericin-B
- » **Antimetabolites:** Methotrexate, Cladribine
- » **Chemotherapeutic agents:** Platinum-based chemotherapeutic agents – Cisplatin, Carboplatin
- » **Anti-inflammatories & immunosuppressants:**
 - » NSAIDs
 - » Cyclosporine
 - » Calcineurin inhibitors
- » **Others:** Inhalational anesthetics, Lithium, Herbal remedies, PPIs (Omeprazole, etc.), phenytoin, ACEIs, Phosphate-containing bowel preparations and radiographic contrast agents.

DIAGNOSTICS APPROACH TO AKI

A diagnosis of acute kidney injury (AKI) can be made based on an acute increase in serum creatinine and/or decrease in urine output in accordance with the definition of AKI.

- » Compare current and previous creatinine levels to determine if the process is acute.
- » Check diagnostic criteria and perform staging of AKI.
- » **Determine the most likely mechanism of AKI (i.e., pre-renal, intrinsic, or post-renal) based on:**
 - » A comprehensive chart review, history, and physical examination
 - » Supportive diagnostic findings and response to initial interventions
- » Consider further testing for specific underlying causes of AKI.

DIAGNOSTIC CRITERIA OF ACUTE KIDNEY INJURY

Acute kidney injury is defined as the presence of any of the following criteria:

- » Increase in serum creatinine by ≥ 0.3 mg/dL ($26.5 \mu\text{mol/L}$) within 48 hours.
- » Increase in serum creatinine to ≥ 1.5 times baseline level within 7 days.
- » Decrease in urine output to < 0.5 mL/kg/hour for ≥ 6 hours.

STAGING OF ACUTE KIDNEY INJURY

The KDIGO stages are widely used and correlate with the risk of death, need for renal replacement therapy, and long-term outcomes (e.g., CKD).

Other classifications include:

» **RIFLE criteria:** A classification system for acute kidney injury

- The acronym stands for Risk, Injury, Failure, Loss, and End-stage kidney disease.
- For the first three categories, patients are classified according to the level of kidney injury (i.e., degree of increase in serum creatinine and/or decrease in GFR and urine output) and for the last two categories, according to the duration of complete loss of kidney function.

» **Acute Kidney Injury Network (AKIN) criteria**

Kidney Disease Improving Global outcomes (KDIGO) criteria for staging of AKI

Stage	Serum creatinine	Urine output
AKI stage 1	» Increase of 0.3 mg/dL ($26.5 \mu\text{mol/L}$) » OR 1.5–1.9 times baseline	» < 0.5 mL/kg/hour for 6–12 hours
AKI stage 2	» 2.0–2.9 times baseline	» < 0.5 mL/kg/hour for ≥ 12 hours
AKI stage 3	» ≥ 3 times baseline » OR increase to ≥ 4 mg/dL ($354 \mu\text{mol/L}$) » OR Renal Replacement Therapy Initiated » OR in patients < 18 years of age: decrease in eGFR to < 35 mL/min/ 1.73 m^2	» < 0.3 mL/kg/hour for ≥ 24 hours » OR anuria for ≥ 12 hours

If serum creatinine and urine output correlate with different stages, consider staging based on the criterion that corresponds to the highest stage

DIAGNOSTIC WORKUP FOR AKI

Initial Evaluation	Additional Evaluation
Laboratory test » Serum creatinine and BUN » Serum electrolytes: sodium, potassium, magnesium, calcium, and phosphate » CBC » Blood gases: ABG (or VBG) » Urinalysis with urine sediment microscopy » Urine sodium, osmolality » Calculate excretion fractions: may help to differentiate prerenal AKI from intrinsic AKI » Fractional excretion of sodium (FENa) » Fractional excretion of urea (FEUrea)	Radiology: Imaging of the kidneys and urinary tract is not necessary to establish a diagnosis of AKI but may be needed to determine the cause » Ultrasound: » Obtain urgently to assess for hydronephrosis in patients with risk factors for urinary tract obstruction » Consider when evaluating renal dysfunction of unclear etiology. » Non-Contrast CT: » Obtain if ultrasound shows hydronephrosis but does not reveal the cause of the obstruction. » Consider when clinical suspicion of obstruction remains high despite the absence of hydronephrosis on ultrasound

Overview of Diagnostic Findings in AKI

Determination of the likely mechanism of Acute Kidney Injury

	Prerenal	Intrinsic	Postrenal
» BUN: creatinine ratio	» $> 20:1$	» $< 15:1$	» Varies
» FENa	» $< 1\%$	» $> 2\text{--}3\%$	
» FEUrea	» $< 35\%$	» $> 50\%$	
» Urine sodium concentration	» < 20 mEq/L	» > 40 mEq/L	» < 350 mOsm/kg
» Urine osmolality	» > 500 mOsm/kg	» < 350 mOsm/kg	
» Urine sediment	» Hyaline casts	» Renal tubular epithelial cells or granular, muddy brown, or pigmented casts (e.g., due to ATN) » RBC casts (e.g., due to glomerulonephritis) » Fatty casts (e.g., due to nephrotic syndrome) » WBC casts (e.g., due to allergic interstitial nephritis)	» Hematuria (stones, bladder cancer, clots) » Absent (neurogenic bladder)



DIAGNOSTIC FINDINGS IN DIFFERENT TYPES OF AKI

△ AKI
c/c:

- » May be asymptomatic.
- » Oliguria or anuria
- » Signs of volume depletion (in prerenal AKI caused by volume loss)
 - Orthostatic or frank hypotension & tachycardia
 - Reduced skin turgor
- » Signs of fluid overload (from Na⁺ and H₂O retention)
 - Peripheral and pulmonary edema
 - Hypertension
 - Heart failure
 - Shortness of breath
- » Signs of uremia
 - Anorexia, nausea
 - Encephalopathy, asterixis
 - Pericarditis
 - Platelet dysfunction
- » Signs of renal obstruction (in post-Renal AKI)
 - Distended bladder
 - Incomplete voiding
 - Pain over the bladder or flanks
 - Fatigue, confusion, and lethargy
- » In severe cases: seizures or coma
- » Affected individuals have a higher risk of secondary infection throughout all phases (most common reason for fatalities).

Early nephrology consultCommon indications

- » Indications for acute dialysis or renal biopsy
- » AKI stage 3
- » Inadequate response to initial treatment
- » Intrinsic AKI
- » Presence of CKD, if:
 - The patient has received a renal transplant
 - CKD category G4 or higher

Prerenal AKI

☞ Blood study findings

- » Elevated serum creatinine
- » Serum BUN: creatinine ratio $\geq 20:1$

☞ Urine study findings

- » Normal urinalysis
- » Low urinary sodium and urea excretion
 - Low fractional excretion of sodium (FENa < 1%)
 - Low fractional excretion of urea (FEUrea < 35%)
- » High urine osmolality (>500 mOsm/kg) and specific gravity (>1.020)
- » Urine sediment: hyaline casts due to concentrated urine in the setting of low renal perfusion

☞ Clinical findings: rapid improvement in renal function following acute intervention

Intrinsic AKI

☞ Blood study findings

- » Elevated serum creatinine concentration & rapidly rising serum creatinine level
- » BUN: creatinine ratio $\leq 15:1$

☞ Urine study findings

- » High urinary sodium and urea excretion
 - High urine sodium concentration (> 40 mEq/L)
 - High fractional excretion of sodium (FENa > 2–3%)
 - High fractional excretion of urea (FEUrea > 50%)
- » Low urine osmolality (< 350 mOsm/kg)
- » Urine sediment: renal tubular epithelial cells or granular, muddy brown or pigmented casts

☞ Biopsy: e.g., in suspected rapidly progressive glomerulonephritis

☞ Clinical findings: lack of response to acute intervention

Postrenal AKI

☞ Blood study findings

- » Elevated serum creatinine concentration in bilateral obstruction
- » BUN:creatinine ratio varies; usually normal (i.e., 10:1–20:1)

☞ Urine study findings

- » Normal urinalysis; e.g., when due to neurogenic bladder
- » Hematuria: e.g., when due to stones, bladder cancer, clots
- » Low urine osmolality (< 350 mOsm/kg)
- » Imaging (renal ultrasound or non-contrast CT scan)
 - Bladder distention, high postvoid residual volume, bilateral hydronephrosis and/or obstructing stones

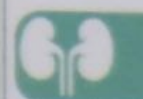
☞ Clinical findings: rapid improvement in renal function following resolution of the obstruction

APPROACH TO THE MANAGEMENT OF AKI

- ☞ Initiate treatment for the underlying cause of AKI based on the presumed mechanism.
 - » Prerenal: Correct adverse hemodynamic factors and replace the depleted volume as needed.
 - » Postrenal: Relieve the urinary tract obstruction.
 - » Intrinsic: Consider a trial of IV fluids; identify and treat underlying causes that require specific interventions.
- ☞ Consider indications for acute dialysis and early nephrology consultation.
- ☞ Provide supportive care to all patients.
 - » Hold potentially nephrotoxic substances, ACEIs, ARBs, NSAIDs, and non-essential medications.
 - » Adjust the dosing of essential renally cleared medications.
 - » Manage volume status and blood pressure to optimize kidney perfusion.
 - » Identify and manage complications: E.g., electrolyte disturbances, acidosis, and fluid overload.
 - » Consider additional supportive care measures: E.g., nutritional support, VTE prophylaxis.
- ☞ Provide patient education and ensure adequate post-discharge follow-up.

TREATMENT FOR THE UNDERLYING CAUSE OF AKI

AKI subtype	Cause	Management
Prerenal	» Hypovolemia	» IV fluid resuscitation with isotonic crystalloids to restore fluid losses
	» Shock	» Immediate hemodynamic support » Identification of the cause of shock
	» Reduced effective arterial volume	» Cardiorenal syndrome: diuretic therapy in acute heart failure » Hepatorenal syndrome management strategies include: ▪ IV albumin, midodrine, and/or octreotide ▪ TIPS for refractory HRS » Specialist consultation (Cardiology, Hepatology, and Nephrology) is advised.
	» Drugs that affect glomerular perfusion	» Discontinuation of offending medications (e.g., ACEIs, ARBs, NSAIDs) » Ensure adequate hydration.
Intrinsic	» Acute tubular necrosis (ATN)	» Discontinuation of potential nephrotoxins » Supportive care of AKI (mainstay of treatment) including IV fluid therapy with isotonic crystalloids ▪ Oliguric phase: Strict fluid balance monitoring to avoid fluid overload ▪ Polyuric phase: Matching of fluid and electrolyte losses to prevent a secondary kidney insult from hypovolemia
	» Acute Interstitial Nephritis (AIN)	» Discontinuation of potential nephrotoxins » Treatment of the underlying etiology » Glucocorticoid therapy may be considered.
	» Contrast-induced nephropathy	» Supportive care of AKI (mainstay of treatment) including prevention of further nephrotoxin exposure » Management of any complications
	» Glomerulonephritis	» Glucocorticoids and/or other immunosuppressive therapy may be considered
	» Vascular cause	» Management of hypertensive crises: e.g., IV antihypertensives » Scleroderma renal crisis: urgent initiation of an ACE-I; captopril is preferred » TTP or HUS management » Plasma exchange therapy » Specialist consultation is advised.
Postrenal	» Bladder outlet obstruction	» Urgent relief of urinary tract obstruction ▪ Urethral catheterization ▪ Consider suprapubic catheterization, if a urethral catheter cannot be passed
	» Ureteral or renal pelvic obstruction	» Urgent urology consults to relieve urinary tract obstruction » Management strategies include: ▪ Ureteral stenting ▪ Percutaneous nephrostomy



Renal replacement therapy

» Indications

Consider urgently for:

- » Complications refractory to medical management
- Refractory fluid overload
- Electrolyte imbalances
- Acid-base disturbances

- » Acute poisoning (e.g., by ethylene glycol); see "Approach to the poisoned patient."
- » Uremic symptoms

» Modalities include:

- Hemodialysis
- and/or hemofiltration (by CRRT or intermittent hemodialysis)
- Peritoneal dialysis

ACUTE KIDNEY INJURY (AKI)

TREATMENT OF ACUTE KIDNEY INJURY (AKI)

Rx

- » Confirm diagnosis: Diagnostic criteria for AKI and stage AKI
- » Obtained labs: CBC, BMP, calcium, phosphate, magnesium, and ABG or VBG
- » Urine studies: urinalysis, urine microscopy, urine chemistry (sodium, urea, osmolality, creatinine)
- » Obtain urgent ultrasound KUB and/or placement of foley's catheterization (if urinary tract obstruction is suspected).
- » Consider early nephrology consult.
- » Optimize volume status.
 - » Consider crystalloid solutions: Balanced IV fluid (Ringer Lactate, Plasma-Lyte A) may be preferred for most patients
 - » Avoid artificial colloids (e.g., hydroxyethyl starch)
 - » Reserve IV albumin for select patients under specialist guidance.
- » Identify and treat any metabolic complications: E.g., acidosis, hyperkalemia
- » Identify and treat the underlying cause (see etiology above)
- » Hold nephrotoxic medications and renally-dose other medications.
- » Strict input/output monitoring
- » Provide additional supportive care
 - » Nutritional support
 - Ensure adequate protein and calorie intake.
 - Consider dietary potassium &/or phosphate restriction for patients with hyperkalemia &/or hyperphosphatemia
 - » Glucose Management: Consider insulin therapy to maintain serum glucose between 110 and 149 mg/L (6.1 and 8.3 mmol/L) in critically ill patients.
 - » Stress ulcer prophylaxis: Consider starting a PPI (Pantoprazole) in critically ill patients who are at risk of GI bleeding.
 - » VTE prophylaxis: If indicated, unfractionated heparin may be preferred over low molecular weight heparin (LMWH) or direct oral anticoagulants (DOACs) in patients with severe renal impairment.
 - » Uremia: Monitor for signs and symptoms; if present, consider renal replacement therapy.



PREVENTION OF ACUTE KIDNEY INJURY

- » Identify patients who are at risk of AKI and implement appropriate preventive strategies.

Risk factors	Preventive strategies
Acute illness	» Consider temporarily holding ACE-Is, ARBs, and diuretics in the setting of vomiting, diarrhea, and/or sepsis » Prevent hypovolemia & hypotension by optimizing fluid volume and hemodynamic status. ▪ Fluid resuscitation: Avoid colloids solution; Balanced crystalloid solutions (e.g., Ringer Lactate, Plasma-Lyte A) are preferred over normal saline ▪ Maintain adequate MAP (> 65 mmHg is appropriate for most patients).
Nephrotoxic medication exposure	» Avoid nephrotoxic medication whenever possible. » Single daily dosing of aminoglycosides is preferred over multiple daily dosing if no suitable antibiotic alternatives are available. » Alternative antifungals (Azoles or echinocandins) or lipid formulations of Amphotericin-B are preferred over conventional Amphotericin-B
Iodinated radio-contrast agent exposure	» Screen for reduced estimated glomerular filtration rate (eGFR) if risk factors are present.
Liver failure	» Recognize and manage ascites, spontaneous bacterial peritonitis, and GI bleeding early » Administer IV albumin supplementation in patients with spontaneous bacterial peritonitis or following large-volume therapeutic paracentesis.
Surgery	» Perioperative management ▪ Optimize fluid volume and hemodynamic status. ▪ Consider holding ACE-Is, ARBs, and diuretics
Endogenous nephrotoxins	» Initiate aggressive IV fluid therapy targeting high urine output



IRON DEFICIENCY ANEMIA (IDA)

INTRODUCTION

- Iron deficiency anemia (IDA) is the most common blood/nutritional disorder worldwide.
- Iron deficiency anemia (IDA) is most common in female 15 – 45 years of reproductive age
- Iron deficiency anemia (IDA) is due to deficiency of iron causing defective heme synthesis.

CAUSES OF IRON DEFICIENCY ANEMIA (IDA)

Decrease intake	Impaired absorption	Increased requirement	Chronic blood loss
- Dietary lack - Poverty - Infants - Elderly	- Steatorrhea - Celiac Sprue - Tropical sprue - Whipples disease - Crohn disease - TB intestine - Chronic diarrhea - Gastroectomy - Duodenal surgery - Duodenal resection	- Growing infants and children - Pregnant females - Premenopausal women	Gastrointestinal Tract » Peptic ulcer » Gastric cancer » Hemorrhoids » Ankylostoma Duodenal (Hookworm) Urinary tract Genital tract Respiratory tract

PATHOGENESIS OF IRON DEFICIENCY ANEMIA (IDA)

- Iron Deficiency Anemia due to decreased synthesis of heme and can be divided into 3 stages.
- Stage 1 (Iron depletion): Iron adequate to maintain normal Hb level and only serum ferritin decreased.
 - Stage 2 (Iron deficient erythropoiesis): Lowering of serum iron and transferrin saturation levels without anemia (Hb, MCV and MCH within normal range). Bone marrow shows iron deficient erythropoiesis.
 - Stage 3 (Iron deficiency anemia): Low serum iron, serum ferritin and transferrin saturation. Impaired hemoglobin production. Morphologically, first reduction in the size

CLINICAL FEATURES OF IRON DEFICIENCY ANEMIA (IDA)

Nonspecific and related to both severity and the cause of the anemia (e.g. gastrointestinal disease)

- Onset: Insidious.
- Nonspecific symptoms:
 - » Chest pain and dyspnea on exertion
 - » Fatigue, palpitations, breathlessness, weakness, and irritability.
 - » Pharyngeal/esophageal webs formed cause dysphagia.

Patterson-Kelly or Plummer-Vinson syndrome:

- » Microcytic hypochromic anemia
- » Atrophic glossitis
- » Esophageal webs

Congestive heart failure is severe anemia.

Central nervous system:

- » Pica-unusual craving for substances with no nutritional value like clay or chalk.
- » Craving for ice (pagophagia) specific to iron deficiency.
- » Pica may be the cause rather than effect of IDA.

Physical Findings

- » Diminished tissue enzymes cause characteristic epithelial changes of iron deficiency anemia.
- » Angular stomatitis and glossitis
- » Chronic atrophic gastritis
- » Koilonychia (spoon nails).

Factors Enhancing Iron Absorption

- » Haem iron, proteins fermentation products, meat, fishmeat, fish
- » Ascorbic acid, citric acid, tartaric acid, gastric acidity.
- » Increased erythropoiesis (high altitude, haemolysis, bleeding)

Factors Inhibiting Iron Absorption

- » Tea, coffee, milk, egg, Zinc
- » Phosphate, Antacids, Herbal drinks
- » Calcium & Calcium rich foods



DIAGNOSIS OF IRON DEFICIENCY ANEMIA (IDA)

1st Step:

- » Confirmation of anemia
 - Hemoglobin (Hb): ↓↓
 - Hematocrit (Hct): ↓↓

2nd Step:

- » Check MCV count: <76 femtoliters (↓↓)
- » Peripheral smear:
 - Microcytic (small) and hypochromic (pale) RBCs
 - Severe anemia shows ring/pessary cells.
 - Moderate anemia anisocytosis and poikilocytosis pencil/cigar-shaped cells.
 - WBCs: Normal; eosinophilia in hookworm infestation.
 - Platelets: Normal

3rd Step:

- » Serum iron profile (iron studies)
 - Reduced: Serum iron, Ferritin, % transferrin receptor saturation.
 - Increased: TIBC, TFR and red cell protoporphyrin

Investigation

- » Complete blood count (CBC)
- » Peripheral smear
- » Iron studies: Ferritin level
- » Ultrasound abdomen

Iron dosage Calculation formula: The total iron deficit calculated with the following formula: Total iron deficit [mg] = body weight [kg] x (target Hb-actual Hb) [g/l] x 0.24* + depot iron [mg]

Rx

Treatment of IDA – Prescription #1

1. Increase consumption of iron-rich diet (meats, iron-fortified food, fresh green leafy vegetables)
2. Treat the underlying disease: Anthelmintics for hookworm, OCPs for menorrhagia.
3. Tab. Ferrous (Iron) Sulphate 200mg (Ferrous sulphate)
Dosage: 60mg to 200mg elemental iron daily
4. Tab. Methyl-Folate 400mcg (Myfol, Adfol, Maxfol, M-Folate)
0-0-1 (OD)

Rx

Treatment of IDA – Prescription #2

1. Tab. Ferrous sulphate 150mg + Folic acid + B-Complex (Fefol, FefolVit, Fervit)
OR Cap. Ferrous (Iron) Sulphate 250mg + B-Complex (Singobion)
OR Tab. Elemental Iron 105mg + Folic acid 800mcg + B-Complex (Iberet-Folic)
OR Tab. Iron Polymaltose 100mg + Folic Acid 0.35mg (Maltofer-Fol, Ferosoft-FA, Malcifer-F, Polymalt-F)
1-0-1 (BD)
OR Symp. Iron Polymaltose 100mg + Folic Acid 0.35mg (Maltofer-Fol, Ferosoft-FA, Malcifer-F, Polymalt-F)
2-0-2 (BD)

Rx

Treatment of IDA – Prescription #3

- » Maintain intravenous (IV) access.
- » Blood transfusion: If Hb <7 – Cross matching with Arrange 2 units of PCVs/RBCs
- » Inj. Iron (Ferric) sucrose (Venofer, Besleri-S, Ferosoft-S) at dose 200mg to 300mg, diluted in 100ml 0.9% NS (Normal saline) regularly for 3 days or on alternative days (Total 3 doses).
OR Inj. Ferric carboxymaltose 500mg/10ml (Fercari, FCM, Elen-Jec), dilute in 100ml 0.9% Normal saline (NS) infuse quickly (using a volumetric infusion pump) over 15 minutes. After infusion flush IV line with 50 ml NS
 - » Dosage: Patients weighing 50 kg or more: Two doses of 750 mg each, 7 days apart.
 - Patients weighing less than 50 kg: Two doses of 15 mg/kg (up to 750 mg per dose), 7 days apart.
- » Inj. Vitamin B1 + B2 + B6 (Neurobion, Neuro-Bedoxine) x IV x STAT on Alternative day x 10 doses

MEGALOBLASTIC ANEMIA

VITAMIN B12 DEFICIENCY ANEMIA

CAUSES VITAMIN B12 DEFICIENCY ANEMIA

1. Decreased intake: Inadequate diet, "pure vegetarians" (vegans)
2. Impaired absorption
 - » Gastric:
 - Deficiency of gastric acid or pepsin or intrinsic factor
 - Pernicious anemia (Autoimmune atrophic gastritis)
Most common cause of vitamin B12 deficiency
 - H. Pylori infection
 - Post-gastrectomy
 - » Intestinal
 - Loss of absorptive surface
 - Malabsorption syndromes: Tropical sprue, celiac sprue
 - Diffuse intestinal disease, e.g. Lymphoma, systemic sclerosis
 - Surgical resection of the ileum - seen in Crohn disease
 - Bacterial or parasitic competition for vitamin B12
 - Bacterial overgrowth in blind loops and diverticula of bowel
 - Fish tapeworm infestation (*Diphyllobothrium latum*) – due to raw fish
 - » Medications (Chronic use): Metformin, H2 receptor antagonists (Famotidine), Proton pump inhibitors (Omeprazole), and anticonvulsants (Carbamazepine)
3. Increased demand:
 - » Pregnancy and breast feeding
 - » Hyperthyroidism
 - » Polycythemia
 - » Increase cell turn over – malignancy of blood cells

CLINICAL FEATURES OF VITAMIN B12 DEFICIENCY ANEMIA

1. Onset: insidious and progresses slowly.
2. Signs of anemia: fatigue, pallor palpitation, dyspnea on exertion
3. Mild scleral icterus and/or jaundice
4. ± Splenomegaly
5. Neurological disturbances are generally symmetrical
 - » Peripheral neuropathy: tingling, numbness, pins-and-needles sensation, coldness (especially in the lower extremities)
 - » Subacute combined degeneration of spinal cord: symmetrical demyelination of the spinal cord tracts occurs in vitamin B12 deficiency due to insufficient vitamin B12-dependent fatty acid synthesis and production/maintenance of myelin
It manifests with the following symptoms:
 - Paresthesia, impaired proprioception, loss of vibratory sensation, tactile sensation, and position discrimination due to demyelination of the dorsal columns
 - Spastic paresis due to demyelination of the lateral corticospinal tracts (axons of UMN)
 - Gait abnormalities (spinal ataxia) resulting from the damage of spinocerebellar tracts and dorsal columns
 - » Neuropsychiatric disease: Reversible Dementia, Depression, Paranoia

FOLIC ACID DEFICIENCY ANEMIA

CAUSES OF FOLIC ACID DEFICIENCY ANEMIA

1. Decreased intake: Inadequate diet—alcoholism, malnutrition
2. Impaired absorption
 - » Malabsorption states: Celiac sprue and tropical sprue

- » Diffuse infiltrative diseases of the small intestine (e.g. lymphoma)
- » Surgical resection of the jejunum
- » Medications:
 - Anticonvulsant: Phenytoin, sodium valproate
 - Oral contraceptives
 - Antifolates/antibiotics: Trimethoprim, sulphonamides
 - Anticancers: Mercaptopurine
- 3. Increased loss: Hemodialysis
- 4. Increased demand: Pregnancy, Lactation, Infancy, Hyperthyroidism, Polycythemia, increase cell turn over (malignancy of blood cells) and Markedly increased hematopoiesis
- 5. Impaired utilization: Folic acid antagonists, such as methotrexate

CLINICAL FEATURES OF FOLIC ACID DEFICIENCY ANEMIA

1. Signs of anemia: Fatigue, pallor, palpitation, dyspnea on exertion
2. Mild scleral icterus and/or jaundice
3. Glossitis
4. ± Splenomegaly
5. ± Bleeding and repeated infections

DIAGNOSIS OF MEGALOBlastic ANEMIA (VITAMIN B12/ FOLIC ACID)

- ❖ Investigation: CBC, Peripheral smear, LFTs, PT & INR, Retic count, Serum LDH, serum Vitamin-B12, serum Folate level and Ultrasound abdomen
- ❖ Blood findings in vitamin B12 and/or folic acid deficiency are similar

1st step:

Confirm anemia	Markers of hemolysis	Ultrasound abdomen
• Hemoglobin (Hb): Decreased • Hematocrit (Hct): Decreased • WBC count (leukopenia): Decreased • Platelet count: Decreased	• LFTs: Only ↑ serum unconjugated bilirubin • Serum LDH: ↑ • Retic count: Normal or low	• Splenomegaly

- » Frequently thrombocytopenia and leukopenia (possibly pancytopenia)
- » Serum iron and serum ferritin - Increased

2nd step

- » Check MCV count: ↑↑↑ (>96 Femtoliters)
- » Peripheral smear:
 - Pancytopenia: Decreased RBC, WBCs and platelets
 - Macrocytic and oval (egg-shaped macro-ovalocytes) - **Diagnostic**
 - Hypersegmented neutrophils (more than five nuclear lobes): First and most specific morphological sign of megaloblastic anemia - **Hallmark feature**
 - Hypersegmented macropolys - These neutrophils are larger than normal
 - Mega platelets

3rd step: Investigation of choice

- ❖ Serum folic acid level: Decreased → Folic acid deficiency anemia
- ❖ Serum vitamin B12 level: Decreased → Vitamin B12 deficiency anemia
 - Normal value of vitamin B12: >240 pg/ml to 1100 pg/ml
 - Borderline level (Possible deficiency): 170-240 pg/ml
 - Vitamin B12 deficiency: <170 pg/ml

If vitamin B12 serum levels are decreased, determine the underlying cause

Test for autoantibodies

- Anti-IF antibodies
 - Antiparietal cell antibodies
- } to rule out Pernicious anemia

If autoantibodies are negative, perform:

- Schilling test: a test to determine the cause of vitamin B12 deficiency
 - Consists of four stages that assess impaired vitamin B12 uptake (see table below)
 - Patients ingest radiolabelled vitamin B12 and then its urinary excretion is measured.

- Urinary excretion of 8–40% (varies between laboratories) of radioactive vitamin B12 within 24 hours is considered normal.
- No longer routinely used in clinical practice
- Gastroscopy/UGI endoscopy + biopsy
- D-xylose absorption test
- Stool examination (ova and cysts)

STAGES OF SCHILLING TEST

Stages	Description	Radiolabeled vitamin B12 measures in urine
Stage 1	» Oral radiolabeled vitamin-B12 1mg PLUS IM dose of unlabeled vitamin-B12 1000mg (saturated transcobalamin injection)	» Normal excretion: Malnutrition or an increased demand is the most likely cause. » Decrease Excretion: perform stage 2
Stage 2	» Oral radiolabeled vitamin-B12 1mg PLUS Intrinsic factor	» Normal excretion: malabsorption due to lack of intrinsic factor » Decrease Excretion: perform stage 3
Stage 3	» Oral radiolabeled vitamin B12 1mg PLUS antibiotics	» Normal excretion: bacterial overgrowth » Decrease Excretion: perform stage 4
Stage 4	» Oral radiolabeled vitamin B12 PLUS pancreatic enzymes	» Normal excretion: lack of pancreatic enzymes (e.g., chronic pancreatitis)

If vitamin B12 serum levels are normal

- Measure homocysteine: elevated in both vitamin B12 deficiency and folate deficiency
- Measure methylmalonic acid (MMA) to help rule out folate deficiency

MMA is normal in folate deficiency and elevated in vitamin B12 deficiency

Treatment of Megaloblastic Anemia

Prescription #1

1. Nutritional counseling to increase folate and B12 intake
 - » Sources of Vitamin B12: Meat, egg, liver and dairy products.
 - » Daily requirement: 2.4 mcg
 - » Sources of Folic acid: Fruits, green leafy vegetables and animal protein.
 - » Daily requirement: 400 mcg
2. Tab. Vitamin B1, B6, B12 (Neurobion, Neuro-Bedoxine)
OR Tab. Methylcobalamin 500 mcg (Methycobal, Cobalamin, Neuromet)
1-0-1 (BD)
3. Tab. Folic acid 5mg
0-0-1 (OD) x Once daily for 3 weeks cures acute deficiency, while 5mg once weekly is sufficient for maintenance therapy.
OR Tab. Methyl-folate 400 mcg (Myfol, Adfol, Maxfol, M-Folate)
0-0-1

Treatment of Megaloblastic Anemia

Prescription #2

- Nutritional counseling to increase folate and B12 intake
- Vitamin B12 deficiency
 - » Inj. Cyanocobalamin + B1 + B2 (Neurobion, Neuro-Bedoxine) x IV x OD for 7 days, then every weekly for 4 weeks then every monthly for the 6 months of duration.
 - OR Inj. Methylcobalamin 500 mcg (Methycobal, Neuromet, Cobalamin) x 2 ampule (=1000mcg = 1mg) x IM, in 5 doses at 2-3 days apart (a total of 5 mg), followed by maintenance therapy of 1000 mcg (1mg) every 3 months for rest of the life.
- Folate deficiency: Tab. Folic acid 5mg x PO x OD daily for 3 weeks cures acute deficiency, while 5 mg once weekly is sufficient for maintenance therapy.
- A sensory neuropathy may take 6-12 weeks to correct, long standing neurological damage may not improve.

ACUTE LEUKEMIA

Clinical features

- ☞ Clinical features are either related to bone marrow failure, infiltration of organs by leukemic cells, or a combination of both.
- ☞ **General features of acute leukemia**
 - » Sudden onset of symptoms and rapid progression (days to weeks)
 - » **Anemia:** Fatigue, pallor, weakness, palpitation, dyspnea on exertion
 - » **Thrombocytopenia:** Epistaxis, bleeding gums, petechiae, purpura or menorrhagia.
 - » **Immature leukocytes:** Fever and frequent infections is due to neutropenia, with the risk of infection rising as the neutrophil count falls below 500/mcL ($0.5 \times 10^9/L$).
 - » **Common presentations include** cellulitis, pneumonia, & perirectal infections; death within a few hours may occur if treatment with appropriate antibiotics is delayed. Fungal infections are also commonly seen
 - » Hepatosplenomegaly (caused by leukemic infiltration)
 - » Oncologic emergencies can be the first sign of leukemia, e.g., an elderly patient presenting with priapism or DIC may have leukostasis (more common in AML than ALL)
- ☞ Fever in a patient with acute leukemia must always be treated as a sign of infection until proven otherwise!
- ☞ Fever and lymphadenopathy are rare in AML but can be common first signs in ALL!

Clinical features of Acute lymphoblastic leukemia (ALL)	Clinical features of Acute myelogenous leukemia (AML)
» Fever, night sweats, unexplained weight loss » Painless lymphadenopathy » Bone pain: Presenting as limping or refusal to bear weight in children » Airway obstruction (stridor, difficulty breathing) due to mediastinal or thymic infiltration (primarily in T-cell ALL) » Features of SVC syndrome » Meningeal leukemia: Headache, neck stiffness, visual field changes » Testicular enlargement (rare finding)	» Leukemia cutis (or myeloid sarcoma): Nodular skin lesions with a purple or gray-blue color » Gingival hyperplasia: AML subtype M4 and M5 » Signs of CNS involvement: Headache, visual field changes (uncommon)

Diagnostic workup of Acute leukemia

1. **Initial routine lab test:** Suspect acute leukemia in patients with suggestive clinical or laboratory features.
 - ☞ Findings on initial laboratory studies are usually nonspecific but may help to identify potentially life-threatening acute complications.
 - ☞ **Complete blood count (CBC)**
 - » **Hemoglobin (Hb):** typically, anemia
 - » **Platelets count:** typically, mild to severe thrombocytopenia
 - » **White blood cell count (WBC):** May be elevated, normal, or low and is not a reliable diagnostic marker.
 - ☞ **Peripheral blood smear:** presence of blasts (immature WBCs)
 - ☞ **Liver function tests and renal function tests:** may be abnormal (e.g., secondary to disease infiltration)
 - ☞ **Comprehensive metabolic panel (CMP) and other metabolic studies (LDH, Uric acid, Calcium, Phosphate)**
 - » Often abnormal due to increased cell lysis
 - » **Common findings include derangements of:**
 - ☞ **Serum Sodium:** Hyponatremia OR Hypernatremia
 - ☞ **Serum Potassium:** Hypokalemia OR Hyperkalemia
 - ☞ **Serum Calcium:** Hypocalcemia OR Hypercalcemia
 - ☞ **Serum Phosphate:** Hypophosphatemia OR Hyperphosphatemia
 - ☞ **Serum LDH:** ↑
 - ☞ **Serum Uric acid:** ↑
 - ☞ **Coagulation profile:** Mild coagulopathy may be present. Studies may also help to identify features of DIC
 - ☞ If DIC is present, the fibrinogen level will be reduced, the prothrombin time prolonged, and fibrin degradation products or fibrin D-dimers present.
2. **Confirmatory diagnostic tests:** Bone marrow aspiration and biopsy
 - ☞ Histopathological features should be assessed using bone marrow aspiration and biopsy.
 - ☞ If unavailable, a peripheral blood smear may be sufficient.

Histopathological features of acute leukemia

	ALL	AML
Blasts in bone marrow or peripheral blood	» > 20% lymphoblasts	» > 20% myeloblasts » Presence of recurrent genetic abnormalities, regardless of the blast percentage: AML : t(8;21), inv(16), or t(16;16), APL : t(15;17)
Cell morphology	» Small- to intermediate-sized blasts » Blasts with large, irregular nuclei (high nuclear-cytoplasmic ratio) » No Auer rods	» Large blasts (2–4 times the size of an RBC) » Blasts with round or kidney-shaped nuclei that contain more cytoplasm than the blasts in ALL » Auer rods (an eosinophilic needle-like inclusion in the cytoplasm), is a characteristic of AML (though sometimes seen in APL, high-grade MDS and myeloproliferative disorders).

3. Specialized Immunophenotype and genetic studies in acute leukemias

Immunophenotype		
Immunohistochemistry	» MPO negative » Terminal deoxynucleotidyl transferase (TdT) positive » Periodic acid-Schiff (PAS): often positive	» MPO positive » TdT negative » PAS negative
Flow cytometry	» B-ALL is usually positive for: 1. CD10 (CALLA): marker for immature B lymphocytes (pre-B), 2. CD19, 3. CD20 » T-ALL is usually positive for CD2–CD8, especially CD3	» The majority of subtypes are positive for CD13, CD33, CD34, CD117, and HLA-DR
Genetic studies		
Cytogenetics (karyotype, FISH)	» Philadelphia translocation: present in ~ 20–30% of adults with ALL but only ~ 5% of children with ALL » Childhood B-ALL t(12;21): most common specific abnormality » Trisomy 4 and 10: associated with a good prognosis » Hyperdiploidy is common in pre-B-ALL	» t(15;17), especially in acute promyelocytic leukemia (M3 AML) » Philadelphia translocation (rare)
PCR (Molecular testing)	» BCR-ABL1 in confirmed or suspected B-ALL » Potential findings in childhood B-ALL include: ▪ t(12;21)(p13.2;q22.1) ▪ ETV6-RUNX1	» FLT3-ITD: associated with a poor prognosis » PML-RARA in patients with APL

4. Screening for extramedullary disease

- Consider the following studies to detect extramedullary disease based on the subtype of acute leukemia and clinical evaluation of the patient: CNS infiltration (common in ALL)
- » Perform a lumbar puncture (Leukemic meningitis) and obtain CSF flow cytometry.
 - » Consider brain and spine CT or MRI
 - » Testicular infiltration (relatively common in ALL): testicular ultrasound
 - » Thymic infiltration (primarily in T-cell ALL): Chest x-ray or CT chest may show a mediastinal mass.
 - » Hepatosplenic infiltration: Abdominal CT or ultrasound may show organ enlargement.
 - » Other forms of extramedullary disease: Consider PET-CT and/or lymph node biopsy



TREATMENT APPROACH OF ACUTE LEUKEMIA

The treatment of acute leukemia is involved different specialties, a hematologist, oncologist, infectious disease specialist depending on the specific subtype and results of molecular testing.

- » **Pretreatment:** All patients should have prechemotherapy screening as part of preparation for cancer treatment.
- » **Chemotherapy**
 - » **Systemic chemotherapy:** The regimen of choice is based on individual patient and disease factors.
 - » **Intrathecal chemotherapy (commonly used):** Consider adding for patients with or at high risk of CNS infiltration (e.g., all patients with ALL).
 - » **Targeted chemotherapy:** Consider adding for leukemias with specific immunophenotype and genetic profiles, e.g., Philadelphia translocation.
- » **Adjunctive treatment,** e.g., radiation therapy, immunotherapy, or stem cell transplantation (SCT): Consider based on individual evaluation.
- » **Supportive care:** Provide holistic care to reduce symptoms and support patients and carers
- » **Management of complications:** Initiate monitoring, prevention, and early aggressive treatment as needed for infection, bleeding, pancytopenia, and oncologic emergencies.
- » **Relapse or refractory leukemia:** Consider re-induction chemotherapy, autologous SCT, or enrollment in a clinical trial in consultation with hematologist-oncologist.

1. Systemic chemotherapy:
 - Regimens vary depending on the subtype of leukemia, the age of the patient, and immunophenotype and genetic study results.
 - » Induction chemotherapy
 - » Average duration for an adult with ALL is 4–8 weeks
 - » Reinduction therapy may be required in case of relapse or failure of primary induction
 - » Consolidation chemotherapy: average duration for an adult with ALL is 4–8 months
 - » Maintenance chemotherapy: average duration for an adult with ALL is 2–3 years

Common agents used in chemotherapy regimens for acute leukemia

- Chemotherapy regimen for Acute lymphoblastic leukemia (ALL)
 - » Alkylating agents: Cyclophosphamide
 - » Anthracyclines: Daunorubicin OR Doxorubicin
 - » Antimetabolites: Cytarabine OR Methotrexate OR 6-mercaptopurine
 - » Enzyme therapy: L-asparaginase
 - » Alkaloids: Vincristine
 - » Corticosteroids: Prednisolone OR Dexamethasone
- Chemotherapy regimen for Acute myelogenous leukemia (AML)
 - » Anthracyclines: Idarubicin OR high-dose daunorubicin
 - » Antimetabolites: Cytarabine OR Methotrexate
 - » Hypomethylating agents: Azacitidine
- Chemotherapy regimen for acute promyelocytic leukemia (APL): If APL is suspected, start treatment early with a differentiation agent (e.g., ATRA) without waiting for immunotype or genetic confirmation. Treatment may be adjusted later depending on the results.
 - » Differentiation agents: to induce the maturation of immature malignant WBCs
 - » ATRA (All-trans retinoic acid)
 - » Arsenic trioxide
 - » Chemotherapy with anthracyclines: e.g., Idarubicin

2. Management of CNS infiltration

- Intrathecal chemotherapy: administration of chemotherapeutic agents (e.g., triple therapy with methotrexate, cytarabine, and hydrocortisone) directly into the subarachnoid space via lumbar puncture or using an intraventricular catheter with a reservoir placed under the scalp
 - » Indications in ALL: Prevention of leukemic meningitis in all patients at the time of diagnosis
 - » Indications in AML
 - Treatment of patients with confirmed CNS infiltration
 - Prevention in patients with high-risk APL
- CNS radiotherapy: Consider directed radiation therapy alongside intrathecal chemotherapy in select patients

3. Advance therapies

- Targeted therapy: Non-standard chemotherapy or immunotherapy is indicated if certain mutations or markers are detected.
 - » Tyrosine kinase inhibitors (TKIs)
 - Philadelphia chromosome-positive ALL: BCR-ABLTKIs, e.g., Imatinib OR Ponatinib
 - FLT3-ITD AML: Consider Midostaurin
 - » Monoclonal antibodies: Rituximab for CD20-positive Philadelphia chromosome-negative ALL, Gemtuzumab ozogamicin for CD33-positive AML
 - » Chimeric antigen receptor T-cell therapy: may be used in ALL
- Autologous or allogeneic stem cell transplantation: Indications include patients with poor prognostic factors (e.g., unfavorable cytogenetics) and those who do not achieve remission with chemotherapy

4. Management of complications

- Oncologic emergencies
 - » Tumor lysis syndrome (TLS)
 - Management: typically includes oral OR IV fluid therapy and Rasburicase.
 - Prophylaxis: Consider hydration, and urate-lowering therapy → Allopurinol OR Rasburicase.
 - » Leukostasis (due to hyperleukocytosis): Consider IV fluid resuscitation and/or cytoreductive therapy.
- Treatment-related complications: Anticancer therapy-induced myelosuppression (anemia (thrombocytopenia, and neutropenia) and mucositis
- Secondary hyperuricemia: Can lead to acute gout, uric acid stones, and urate nephropathy
 - » Consider hydration, fluid administration, and urate-lowering therapy (e.g., allopurinol and rasburicase) as prophylaxis prior to chemotherapy.
- Treatment of specific chemotherapy toxicity

THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP)

△ TTP

C/C:

TTP patients are typically previously healthy adults.

The classic pentad of clinical presentation is consists of:

1. Fever
2. Neurological features
 - » Altered mental status
 - » Delirium, Seizure
 - » Focal defects, stroke
 - » Headache, dizziness
3. ↓ Platelet count (thrombocytopenia)
 - » Petechiae, purpura
 - » Mucosal bleeding
 - » Prolonged bleeding after minor cuts
4. Microangiopathic hemolytic anemia
 - » Fatigue, dyspnea, and pallor
 - » Jaundice
5. Impaired renal function
 - » Hematuria, proteinuria
 - » Oliguria, anuria

Additional Investigation:

- » Urinalysis: Hematuria, proteinuria
- » ADAMTS13 activity and inhibitor testing: ↓ ADAMTS13 activity.
- » PT & APTT: While PT and aPTT are normal or only mildly elevated in TTP and HUS (no consumption coagulopathy), they are markedly elevated in DIC (consumption of platelets and all coagulation factors).

NOTE: Platelet transfusion should only be reserved for patients who are bleeding or require an invasive procedure

Rx

1. **Airway:**
 - » Ensure patient is maintaining own airway
 - » Assess and secure stable airway
2. **Breathing:** Check SpO₂ & Give high flow O₂ as appropriate
3. **Circulation:**
 - » Maintain intravenous (IV) access
 - » Start 0.9% Normal Saline (0.9% N/S) x IV x OD
 - » **Vitals monitoring:** Check BP, PR, RR, Temperature, SpO₂
 - » **Send labs:** CBC (Hb ↓, Platelets ↓), reticulocytes ↑, heptoglobin ↓, Peripheral smear: ↑ schistocytes (up to 10% of RBCs and Low platelets), ↑LDH, ↑ indirect bilirubin (hemolytic anemia) Blood urea & creatinine ↑)
 - » **Avoid Platelets transfusion if possible**
 - » Prompt initiation of plasma exchange therapy (PEX) x 5-6L per day for 3-5 days/until platelets are higher & LDH normal
 - » **Consider:** Glucocorticoids – Prednisolone 1-2mg/kg/day
 - » **Inj. Neurobion 1 ampule** x IV x OD
 - » **Inj. 5% D/W 1000ml** x IV x OD
 - » **Inj. Omeprazole 40mg** (Risek, Ruling) x IV x OD
 - » **Inj. Ceftriaxone 1g** (Oxidil, Rocephin, Titan) x IV x BD
 - » **Fever:** Inj. Paracetamol 1g/100ml (Provas) IV infusion x SOS
 - » **Severe Cases:** Inj Rituximab (Ristova)
4. **Disability & Exposure**
 - ☞ Treatment should be started after a presumptive diagnosis is made based on clinical features and initial labs (e.g., blood count, peripheral smear, and creatinine).
 - ☞ **Precautions:** Avoid Intramuscular injection, tooth brushing, shaving and combing as risk of bleeding. Restrict activities to minimise the risk of head injury avoid contact sports, limit activities that have a risk for traumatic injury, Avoid antiplatelet (aspirin/clopidogrel), anticoagulants (Heparin/warfarin), NSAIDs and corticosteroids.
 - ☞ **Monitoring and correction**
 - Fluid status abnormalities
 - Electrolyte disturbances
 - Acid-base abnormalities
 - RBC transfusions
 - ☞ **Prognosis:** Depends primarily on prompt initiation of treatment. Timely treatment can prevent acute complications (AKI, coma, and death), as well as progression to chronic renal failure. The mortality rate of TTP is favorable with treatment: 10–20%



IMMUNE THROMBOCYTOPENIC PURPURA (ITP)

Definition: Immune thrombocytopenia characterized by the autoimmune destruction of platelets, has previously been referred to as idiopathic thrombocytopenic purpura, however, this term is outdated.

- ☞ **Primary immune thrombocytopenia:** an autoimmune disorder characterized by isolated thrombocytopenia ($< 100,000/\text{mm}^3$) with no known precipitating cause
- ☞ **Secondary immune thrombocytopenia:** an autoimmune hematologic disorder causing isolated thrombocytopenia that is secondary to an identifiable trigger
- ☞ **Newly diagnosed ITP:** all cases within the first 3 months of diagnosis
- ☞ **Persistent ITP:** ITP lasting 3–12 months
- ☞ **Chronic ITP:** ITP lasting > 12 months

Pathophysiology

- ☞ Antiplatelet antibodies (mostly IgG directed against, e.g., GpIb/IIIa, GpIb/IX) bind to surface proteins on platelets $\rightarrow$ sequestration by spleen and liver $\rightarrow$ $\downarrow$ platelet count $\rightarrow$ bone marrow megakaryocytes and platelet production increase in response (in most cases)

Etiology

- ☞ **Primary ITP:** Idiopathic (most common cause)
- ☞ **Secondary ITP associated with:**
 - ☞ **Autoimmune disorders:** SLE, Antiphospholipid syndrome
 - ☞ **Malignancy:** Lymphoma (Lymphoproliferative disease), Leukemia (particularly CLL)
 - ☞ **Infection:** Hepatitis-C virus (HCV), HIV, and *H. pylori*
 - ☞ **Medications:** Quinine, Beta-lactam antibiotics, Ceftriaxone, Heparin, Linezolid, sulfonamides, vancomycin, antiepileptics (Carbamazepine), Trimethoprim-sulfamethoxazole (TMP-SMX), also known as co-trimoxazole (Septran), vaccines (also exacerbated by SARS-CoV-2 vaccination). CMDT-2023

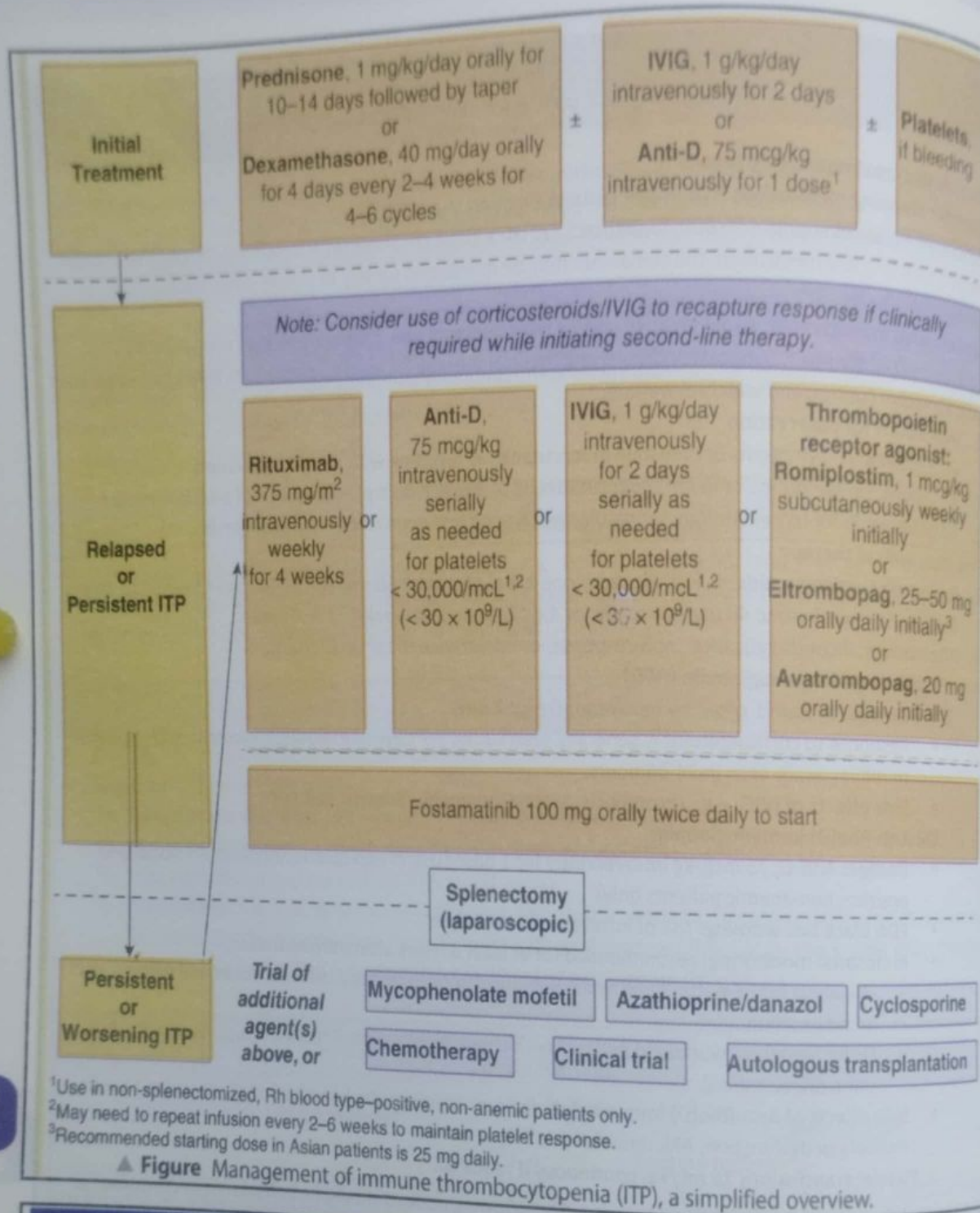
Clinical features

Clinical features	Investigation
Clinical features can correlate with platelet count, ITP is a diagnosis of exclusion; patients typically have a low platelet count with no other abnormalities. ☞ Most commonly » Asymptomatic » Splenomegaly: Typically, absent ☞ Minor mucocutaneous bleeding (less common) » Subcutaneous: Bruising, petechiae, purpura » Mucosal: Mild epistaxis, gingival bleeding ☞ Other types of bleeding (rare) » Gastrointestinal: Melena » Genitourinary: Hematuria, menorrhagia » CNS: features of intracranial hemorrhage » Prolonged OR excessive traumatic bleeding or surgical bleeding ☞ Individuals with secondary ITP (such as due to autoimmune disease, HIV or HCV infection, SLE, or lymphoproliferative malignancy) may have additional disease-specific findings.	Routine testing ☞ CBC: $\downarrow$ Platelet count ($< 100,000/\text{mm}^3$) ☞ Coagulation profile: Usually normal ☞ Bleeding time: May be prolonged ☞ Peripheral blood smear: Normal to large platelets Additional investigations ☞ All adults: HIV and HCV screening ☞ Bone marrow biopsy $\rightarrow$ Consider in atypical cases OR if there is diagnostic uncertainty. ☞ Findings: normal or $\uparrow$ megakaryocytes ☞ Additional testing as required: Consider in suspected secondary ITP, e.g., antinuclear antibodies (ANA) in SLE or <i>H. pylori</i> testing if the patient has gastro-intestinal (GI) symptoms or is from a high prevalence area.

TREATMENT OF ITP

(see Emergency section for severe/life threatening cases)

- Identify and treat underlying causes.
- Consider stopping medications that impair platelet function, e.g., NSAIDs.
- Patient with platelet counts $< 25,000$ - $30,000/\text{mL}$ (25 - $30 \times 10^9/\text{L}$) or those with significant bleeding should be treated with first line medication; the remainder may be monitored serially or progression, but that is a patient-specific decision.
- **Conservative management:** Avoid invasive and/or risky interventions. Examples include nonoperative management of classically surgical conditions and medical therapy focused on preventive measures, supportive care, symptom control, and watchful waiting.
- **Indications for observation**
 - » **Children:** no symptoms or only mild mucocutaneous bleeding with any platelet count
 - » **Adults:** no symptoms or minor mucocutaneous bleeding with a platelet count of $\geq 30,000/\text{mm}^3$
- **All patients:** Refer to hematology for regular monitoring and counseling on bleeding risks.
- **First-line medical therapy**
 - **Preferred: Corticosteroids** → Tab. Prednisolone 1 - 2 mg/kg (max 60 mg) for 10 - 14 days followed by taper OR Tab. Dexamethasone 40 mg/day orally for 4 days every 2 - 4 weeks for 4 - 6 cycles.
 - **Alternatives:** if contraindication, non-response, or intolerance to corticosteroids.
 - » **Intravenous immunoglobulin (IVIG)**
 - **Dosage:** at dose 1 g/kg/day intravenously for 2 days
 - Response to corticosteroids is generally seen within 3 - 7 days of initiating treatment, with response to IVIG typically seen in 24 - 36 hours.
 - **Side effects of IVIG:** e.g., thrombosis, aseptic meningitis, infusion reactions
 - » **OR Anti-Rho(D) immunoglobulin**
 - **Dosage:** Anti-D, 75 mcg/kg intravenously for 1 dose (Use in non-splenectomized, Rh blood type-positive, non-anemic patients only)
 - **FDA black box warning:** risk of intravascular hemolysis
 - **In-hospital monitoring:** recommended for at least 8 hours after administration.
 - Urinalysis for hematuria and hemoglobinuria prior to therapy, and at 2 hours and 4 hours after administration.
 - Order hemolysis workup in patients with characteristic clinical features (e.g., back pain, chills, urine discoloration)
 - **Side effects of Anti-Rho(D) immunoglobulin:** e.g., intravascular hemolysis that can cause anemia, multiorgan dysfunction, AKI, renal failure, DIC, or death.
 - » $\pm$ Platelet transfusions 20 mL/kg , continuous if required.
- **Subsequent therapeutic options:** If no response. The following options should be considered in consultation with a specialist for patients with newly diagnosed immune thrombocyte purpura (ITP) refractory to first-line medical therapy, or relapsed/persistent/chronic immune thrombocyte purpura (ITP).
 - **Thrombopoietin receptor agonists (TPO-RAs)**
 - » Inj. Romiplostim 125 mcg or 250 mcg or 500 mcg (Nplate) $\times 1 \text{ mcg/kg}$ subcutaneously weekly initially
 - » Tab. Eltrombopag 25 mg or 50 mg (Revolade) $\times 25$ - 50 mg orally daily initially
 - » Tab. Avatrombopag 20 mg (Doptelet, Avalet) $\times 20 \text{ mg}$ orally daily initially
 - Inj. Rituximab 500 mg (Ristova, MebThera) $\times$ at dose 375 mg/m^2 IV weekly for 4 weeks. May need to repeat infusion every 2 - 6 weeks to maintain platelet response.
 - **Syk inhibitor:** Tab. Osimatinib at dose 100 mg orally twice daily treats patients with ITP who do not respond to corticosteroids, TPO mimetics, or rituximab.
- **Splenectomy**
 - » **Indications**
 - Treatment-resistant thrombocytopenia lasting > 12 months.
 - Severe bleeding that does not respond to any other treatment.
 - » **Procedure:** Minimally invasive laparoscopic surgery is preferred.



HEMOPHILIAS

- Definition: Hemophilias are disorders of blood clotting and consequently may lead to serious bleeding. In the majority of cases, these disorders are hereditary. The mode of inheritance of hemophilia is X-linked recessive.
- Epidemiology: Affects = 1/5,000 male births. Average age at diagnosis is 1 month for people with severe hemophilia, 8 months for people with moderate hemophilia, and 36 months for people with mild hemophilia.
- Three types of hemophilia, determined based on which clotting factor is deficient:
 - Hemophilia-A (Classic hemophilia) is due to deficiency of – Factor VIII (Commonest type)
 - Hemophilia-B (Christmas disease) is due to deficiency of – Factor IX
 - Hemophilia-C (Rosenthal syndrome) is due to deficiency of – Factor XI

CLINICAL FEATURES

- Spontaneous bleeding or delayed-onset bleeding (joints, muscular and soft tissue, mucosa) in response to different degrees of trauma.
 - Repeated hemarthrosis (bleeding into knee joint) → hemophilic arthropathy (destruction of the joint due to repeated hemarthrosis)

- Typically develops by early adulthood.
- Most commonly involves the knees, ankles, and elbows.
- Recurrent bruising or hematoma formation
- Oral mucosa bleeding, epistaxis, excessive bleeding following small procedures (e.g., dentist procedures)
- Hemophilia-C doesn't typically manifest with spontaneous bleeding, hemarthrosis, or deep tissue bleeding.
- Further sites/symptoms of hemorrhage:** CNS (Headache, neck stiffness), Gastrointestinal tract (Melena, hematemesis), Genitourinary system (Hematuria)
- Female carriers may show mild symptoms.
- The degree of bleeding and, therefore, severity of hemophilia depends on residual factor activity levels; normal reference activity is $> 50\%$.

Severity	Clinical signs	Factor VIII or IX activity
Mild hemophilia	» Hematomas following severe trauma	» $> 5\%$ to $< 50\%$
Moderate hemophilia	» Hematomas following mild trauma	» $\geq 1\%$ to 5%
Severe hemophilia	» Spontaneous hematomas	» $< 1\%$

DIAGNOSTIC WORKUP

- Patient and family history**
- Obtained CBC, Coagulation profile.
- Genetic testing
- Screening
 - Platelet count and Prothrombin time: Normal
 - Activated partial thromboplastin time (aPTT): **Usually prolonged.**
 - If aPTT prolonged $\rightarrow$ mixing study, If mixing study is positive (or if patient/family history are strongly positive) $\rightarrow$ quantitative assessment of factor activity levels $\rightarrow$ send factor VIII level, if negative, send factor IX level
- Investigation of choice (IOC) for hemophilias:** Hemophilia-A = Serum factor VIII level, Hemophilia-B = Serum factor IX level and Hemophilia-C = Serum factor XI level



TREATMENT OF HEMOPHILIA

- Substitution of clotting factors** (Plasma-derived or recombinant factor)
 - Mild or moderate hemophilia:** When needed (E.g., Trauma or surgery)
 - Severe hemophilia:** Prophylactic (additional substitution may be needed in, e.g., trauma)
 - Hemophilia-A:** Factor VIII concentrate and DDAVP
 - Dosage of Factor VIII** at dose 50 units/kg x IV initially followed by 25 units/kg every 8 hours followed by lesser doses at longer intervals once hemostasis has been established.
 - Dosage of DDAVP** at dose 0.3 mcg/kg x IV in 50 mL saline over 20 minutes, or nasal spray 300 mcg for weight > 50 kg or 150 mcg for < 50 kg, every 24 hrs., maximum of three doses in a 72-hour period. If > 2 doses are used in a 48-hour period, free water restriction and monitoring for hyponatremia is essential
 - Hemophilia-B:** Factor IX concentrate
 - Dosage of Factor IX product** at dose 100 units/kg (120 units/kg if using Benefix) intravenously initially for severe hemophilia B followed by 50 units/kg (60 units/kg if using Benefix) every 8 hours followed by lesser doses at longer intervals once hemostasis has been established.
 - Hemophilia-C:** Factor XI concentrate, or FFP or EACA (Epsilon-aminocaproic acid)
 - FFP is typically administered in 4-unit boluses and may not need to be re-bolused after the initial administration due to the long half-life of factor XI
 - EACA dose is 50 mg/kg orally four times daily for 3–5 days; maximum 24 g/day, useful for mucosal bleeding/dental procedures.
- Mild hemophilia A: Desmopressin** (Synthetic analog of vasopressin, abbreviated DDAVP)
- Antifibrinolytic therapy:** Aminocaproic acid & Tranexamic acid (Transamin), Used in addition to factor substitution (e.g., if surgery is performed in the oral cavity). Inhibits the breakdown of clots to reduce the risk of bleeding.
- Emicizumab $\rightarrow$**
 - Therapeutically use in Hemophilia-A**
 - Description:** a humanized monoclonal bispecific antibody that reduces the risk of bleeding events
 - Mechanism of action:** Bridges activated factor IX and factor X by binding to both factors (thereby replacing the deficient factor VIII) $\rightarrow$ activation of factor X $\rightarrow$ restored clotting cascade



APLASTIC ANEMIA

Definition: Aplastic anemia is a condition of bone marrow failure that arises from suppression of, or injury to, the hematopoietic stem cell. The bone marrow becomes hypoplastic, fails to produce mature blood cells, and pancytopenia develops. Aplastic anemia should not be confused with aplastic crisis, a condition in which erythropoiesis is temporarily suppressed (e.g., due to parvovirus B19 infection in patients with hemolytic anemia).

ETIOLOGY

- ☞ **Autoimmune:** Idiopathic in > 50% of cases, SLE, Hepatitis-associated aplastic anemia
- ☞ **Congenital:** Defects in telomere length maintenance or DNA repair (Dyskeratosis congenita, Fanconi anemia)
- ☞ **Medication induced:** Carbamazepine, Methimazole, NSAIDs, Chloramphenicol, Propylthiouracil, sulfa drugs, Cytostatic drugs (esp. alkylating agents and antimetabolites), Gold salt, Phenytoin, Quinacrine, Tolbutamide
- ☞ **Toxins:** Benzene, toluene, insecticides, cleaning solvents.
- ☞ **Ionizing radiation and cytotoxic chemotherapy**
- ☞ **Viruses:** Parvovirus B19, HBV, EBV, CMV, HIV
- ☞ **Malignancy:** Large granular lymphocytic leukemia (T-LGL)
- ☞ **Other:** Pregnancy, Paroxysmal nocturnal hemoglobinuria (PNH)

CLINICAL FEATURES

- ☞ **Symptoms/physical exam:** Insidious onset, but often initial symptoms are due to anemia or bleeding
- ☞ **Sign of Anemia:** Fatigue, pallor, palpitation, dyspnea on exertion
- ☞ **Thrombocytopenia:** Mucosal Bleeding, bruising, Petechiae
- ☞ **Leukopenia:** Infections

DIAGNOSTIC WORKUP

- ☞ **Complete blood count (CBC):** Pancytopenia (in contrast to aplastic crisis characterized by anemia only)
 - » Normocytic anemia or macrocytic anemia
 - » Anemia: Hemoglobin (Hb) ↓↓ with MCV ↑ (Mild macrocytosis)
 - » Leukopenia: WBCs ↓↓
 - » Neutropenia: Neutrophil ↓↓
- ☞ Reticulocyte count: Low
- ☞ EPO level: High
- ☞ **Confirmatory investigation:** Bone marrow biopsy (Findings: Hypocellular bone marrow with fatty infiltration/fat-filled marrow (dry bone marrow tap). RBCs normal morphology).
- ☞ **Investigation for underlying etiology:**
 - » Consider serum B12, serum folate levels, serum ferritin level, LFTs, LDH, and haptoglobin.
 - » **Serological test:** Hepatitis-A, B & C, HIV, EBV, parvovirus, and CMV
 - » **SLE screening:** ANA and/or with reflex to anti-double-stranded DNA if positive

Rx

TREATMENT OF MILD IDIOPATHIC APLASTIC ANEMIA

- ☞ Hospitalized the patient.
- ☞ Withdrawal/stop causative agent if applicable.
- ☞ Established intravenous (IV) access.
- ☞ IV fluid therapy: Start 0.9% Normal saline (NS) or 5% Dextrose x IV x BOLUS.
- ☞ Vitals monitoring: Check B.P, P.R, R.R, Temperature, SpO₂
- ☞ Obtained labs: CBC, LFTs, BUN, Electrolytes, Reticulocytes, Erythropoietin, LDH, heptoglobin & viral workup
- ☞ PCVs/whole blood transfusion: If Hb < 7, advise for blood grouping and cross matching
- ☞ Platelets transfusion: if platelets count is ≤10,000 to 20,000 or there is any evidence of bleeding from any site with thrombocytopenia.
- ☞ Bone marrow stimulants with Epoetin or Darbepoetin, or Filgrastim or Sargramostim or Eltrombopag
 - ☞ Inj. Epoetin Alfa 2000IU or 4000IU or 10,000IU (Epogen, Eprex, Epokine, Mac-Epo, Ropo) x IV/SC
 - ☞ OR Inj. Filgrastim 300mcg (Filgen, Grastin, Neofil, Filatil) x IV/SC
 - ☞ OR Tab. Eltrombopag 25mg or 50mg (Revolade) x PO x OD
- ☞ Antibiotics for secondary bacterial infection: Inj. Ceftriaxone 1 – 2 g (Oxidil, Rocephin) x IV x OD
- ☞ Consider vitamin B1, B6 & B12: Inj. Neurobion 1 Ampule x IV x OD.
- ☞ Gastroprotective: Inj. Omeprazole 40mg/vial (Ruling, Omezol) x IV x OD.

TREATMENT OF SEVERE APLASTIC ANEMIA



- Severe aplastic anemia is defined by a neutrophil count of less than 500/mcL ($0.5 \times 10^9/L$), platelets less than 20,000/mcL ($20 \times 10^9/L$), reticulocytes less than 1%, and bone marrow cellularity less than 20%.
- Curative treatment – Bone marrow transplant (BMT) is treatment of choice for healthy young adult patients under 40 years of age who have an HLA-matched sibling is allogeneic bone marrow transplantation
- Children or young adults may also benefit from **allogeneic bone marrow transplantation** using an unrelated donor. Because of the increased risks associated with unrelated donor allogeneic bone marrow transplantation compared to sibling donors, this treatment is usually reserved for patients who have not responded to immunosuppressive therapy.
- For adults over age 40 years or those without HLA matched hematopoietic stem cell donors, the treatment of choice for severe immunosuppression and hematopoietic stimulation with Antithymocyte globulin (ATG) PLUS Cyclosporine PLUS Eltrombopag – response rates approaching 90%.
- Equine ATG is given in the hospital in conjunction with transfusion and antibiotic support.
- Recommended proven regimen:
 - » Equine Antithymocyte globulin (ATG) at dose 40mg/kg/day x IV for 4 days
 - » AND Tab. Cyclosporine 50mg or 100mg (Sandimmun Neoral 25mg or 100mg, Cipol-N) at dose 6mg/kg x per orally twice daily (BD)
 - » PLUS Tab. Eltrombopag 50mg (Revolade) at dose 150 mg x per orally daily (OD).
 - » ADJUNCT, Corticosteroids ATG with combination of Tab. Prednisolone 5mg (Deltacortril, Rapicort) at dose 1–2 mg/kg/day orally for 1 week, followed by a taper over 2 weeks) to avoid ATG infusion reactions and serum sickness. Responses usually occur in 1–3 months and are usually only partial, but the blood counts rise high enough to give patients a safe and transfusion-free life.
- NOTE: The full benefit of immunosuppression is generally assessed at 4 months post-equine ATG. Cyclosporine and eltrombopag are maintained at full doses for 6 months and then stopped in responding patients. Androgens have been widely used in the past, with a low response rate, and may be considered in mild cases such as Tab. Fluoxymesterone 5mg at dose 10–20 mg/day orally in divided doses or Tab. Danazol 200 mg (Danzol) x orally twice daily (BD)
- IV fluid therapy: R/L, 0.9% N/S or D5%W x IV x BLOUS
- Consider blood and Platelets transfusion
- Antibiotics for secondary bacterial infection: Inj. Ceftriaxone 1 – 2 g (Oxidil, Rocephin) x IV x OD
- Consider vitamin B1, B6 & B12: Inj. Neurobion 1 Ampule x IV x OD
- Gastroprotective: Inj. Omeprazole 40mg/vial (Ruling, Omezol) x IV x OD
- Iron chelation therapy (Deferoxamine) should be considered when the serum ferritin is $>1000 \mu g/L$.
- Advise multivitamins: Tab. Vitrum OR Tab. Revital multi x PO x OD
- Precautions:
 - » Avoid IM injection, tooth brushing, shaving & combing as risk of bleeding.
 - » Avoid antiplatelet agent (aspirin, clopidogrel), anticoagulants (Heparin, Warfarin) & NSAIDs
- COURSE & PROGNOSIS APLASTIC ANEMIA:**
 - » Patients with severe aplastic anemia rapidly have fatal illness if left untreated.
 - » Allogeneic bone marrow transplant from an HLA-matched sibling donor produces survival rates of over 80% in recipients under 20 years old and of about 65 – 70% in those 20 to 50 years old.
 - » Respective survival rates drop by 10 – 15% when the donor is HLA matched but unrelated.
 - » Equine ATG-cyclosporine immunosuppressive treatment leads to a response in approximately 70% of patients (including those with hepatitis virus-associated aplastic anemia) and in up to 90% of patients with the addition of Eltrombopag.



THALASSEMIAS

Definition: Thalassemia is a group of autosomal recessive inherited disorders which is characterized by group of diseases having quantitative defect/ abnormality in globin chains production leading to ineffective erythropoiesis PLUS Extra vascular hemolysis.

- » It is the most common type of hemoglobinopathy in the world.
- » Beta "β" and Alpha "α" thalassemia is caused by deficient synthesis of "β" and "α" chains respectively.
- » **Genetics:** α or β-globin chain of adult hemoglobin (HbA → α₂β₂)
- » The 4 α-globin chain is coded by a gene located on chromosome 16.
- » The 2 β-globin chain is coded by a gene located on chromosome 11.

Causes of thalassemia

- » Point mutation (> 100 types)
- » Three are commonest: 1. Chain Terminator mutation, 2. Splicing mutation, 3. Promotor

Classification of thalassemia

They are mainly classified as:

- » **β-Thalassemia syndromes:** Impaired synthesis of β-chains of globin.
- » **α-Thalassemia syndromes:** Impaired synthesis of α-chains of globin.

Clinical and genetic classification of thalassemias

BETA THALASSEMIA		
Clinical syndromes	Genotype	Clinical features
» β-thalassemia minor/trait	β ^o /β or β ⁺ /β	» Mild anemia and asymptomatic » HbF (0 – 5%) and HbA ₂ 3.6 to 8%)
» β-thalassemia major	β ^o /β ^o or β ⁺ /β ⁺	» Severe anemia (also called Cooley anemia, Mediterranean anemia & von Jaksch anemia) » High level of HbF (30 to 90%) in the blood » HbA ₂ (<3.5%)

ALPHA THALASSEMIA		
Clinical syndrome	No. of α-globin deleted	Clinico-pathological features
» α-thalassemia silent carrier (One gene deletion)	$\frac{\alpha\alpha}{\alpha\alpha}$	» Asymptomatic
» α-thalassemia minor/trait [Two gene deletion (Cis/Trans)]	$\frac{\alpha\alpha}{\alpha\alpha}$ or $\frac{\alpha\alpha}{\alpha\alpha}$	» Usually asymptomatic » Normal hemoglobin level or minimal anemia
» α-thalassemia major (Three gene deletion)	$\frac{\alpha\alpha}{\alpha\alpha}$	» Hemoglobin-H disease » Moderate microcytic, hypochromic anemia
» Hydrops fetalis (Hb Barts) (Four gene deletion)	$\frac{\alpha\alpha}{\alpha\alpha}$	» Severe form, Fatal and usually » Results in intrauterine death

CLINICAL FEATURES OF THALASSEMIA

- » **Age:** Infants develop moderate to severe anemia 6 – 9 months after birth.
- » **Growth and development:** Untreated children fail to thrive and die within 4 – 5 years of age.
- » **Musculoskeletal deformities:**
 - Bone pain
 - Skull: widening of the diploic space "hair on end" appearance and facial bones deformity on skull x-ray
 - **Chipmunk facies**
- » **Severe anemia and Jaundice**
- » **Marked splenomegaly:** Up to 1500 grams due to hyperplasia and extramedullary hematopoiesis.
- » **Extramedullary hemopoiesis:** Liver and lymph nodes may show extramedullary hematopoiesis.
- » **Iron overload:** Multiple blood transfusions may lead to iron overload and result in hemosiderosis and secondary hemochromatosis (Heart, Liver and Pancreas)
- » **Family history (KEY FACTOR):** The risk for beta-thalassemia major, an autosomal recessive genetic condition, is 25% for each pregnancy when both parents are heterozygous for beta-thalassemia mutations. Beta-thalassemia major or trait, need for blood transfusions, or anemia, often specifically unresponsive to iron therapy, in family members. **Risk factors include** Family history of thalassemia, Blood disorder, repeated blood transfusion and splenectomies (increased risk of parvovirus B19 induced crisis).

DIAGNOSTIC WORKUP

- Complete blood count (CBC):
 - Hemoglobin level: ↓ (variable depends on subtype)
 - Microcytic hypochromic anemia → confirmed by low MCV count (< 80 fL) and low MCH (< 27 pg/cell)
 - RDW: normal. ↳ Microcytic (small RBCs = Microcytosis) and hypochromic (pale RBCs)
 - RBC count: Elevated (level higher than iron deficiency anemia)
 - Mentzer index (MCV/RBC ratio): MCV ÷ RBC count → used to differentiate between thalassemia and iron deficiency anemia (IDA). If mentzer index ratio < 13 suggests thalassemia; a ratio > 13 suggests IDA.
 - MCV ÷ RBC count: $58.9 \div 4.2 = 14$, most likely iron deficiency anemia (IDA).
 - MCV ÷ RBC count: $55.8 \div 4.9 = 11.38$, most likely thalassemia.
- Markers of hemolysis: Haptoglobin ↓, serum LDH ↑, Reticulocytes count ↑ and unconjugated bilirubin ↑
- Peripheral blood smear: Target cells (codocytes), Teardrop cells, Anisocytosis and poikilocytosis (anisopoikilocytosis), HbH inclusion bodies, Erythroblasts & Elevated WBCs (Leukocytosis with mild left shift)
- Confirmatory test of choice: Hb electrophoresis should be performed in all patients → Hb Electrophoresis (Qualitative analysis) OR Hb Electrophoresis with HPLC (Qualitative + Quantitative analysis)
- Interpretation of Hb Electrophoresis: Normal values: HbA (97-99%), HbA₂ (1-3%) & HbF < 1% (CMTD-2024)
 1. Alpha thalassemia: presence of HbH, Hb Bart, & concomitant hemoglobinopathies (HbE, HbS, HbC, HbD)
 2. Beta-thalassemia minor/trait: Slightly decrease HbA and elevated HbA₂ and High HbF
 3. Beta-thalassemia intermedia: Decrease HbA and elevated HbA₂ and HbF
 4. Beta-thalassemia major: Elevated HbA₂ and HbF with little or No HbA

TREATMENT OF THALASSEMIA

- All patients of thalassemia: Patient education and genetic counseling. Screening tests for relatives
- Thalassemia minor/trait: Usually no treatment/transfusion required. Iron supplementation, Episodic folic acid supplementation may be indicated (e.g., during pregnancy, acute infections) & Genetic counselling.
- Thalassemia major and thalassemia intermedia
 - Blood transfusion therapy → requires informed consent.
 - Indication (for transfusion-dependent thalassemias): Hb < 7 g/dL &/or marked clinical symptoms.
 - Target hemoglobin: Hb > 9 to 10 g/dL.
 - N.B. Parents and first-degree relatives should not be blood donors for these candidates. Before the first transfusion, patients' RBCs are typed for Rh and ABO antigens. At the same time, cytomegalovirus (CMV) status should be obtained.
 - Surveillance and treatment of complications
 - Iron overload diseases: All patients receiving transfusion therapy should be periodically evaluated for iron overload disease and subsequent organ damage.
 - Clinical features: Bronze skin, growth delay, signs of organ damage.
 - Diagnosis: Liver iron concentration (LIC) measured by Liver biopsy (gold standard test) or MRI
 - General monitoring: Serum ferritin
 - Monitoring for organ damage:
 - Endocrinopathies: Screen patients for the following conditions and refer to endocrinology as needed: Diabetes, Hypothyroidism/hypoparathyroidism, Hypogonadism and Osteoporosis
 - Liver cirrhosis and hepatocellular carcinoma (HCC): LFTs (every 3 months) & MRI (annually)
 - Cardiac siderosis: regular radiological test (Echocardiogram or MRI)
 - Treatment: Chelation therapy is typically recommended when iron accumulates to toxic levels & may be required from a very early age. Deferoxamine (SC, IM, IV), Deferasirox (PO), Deferiprone (PO)
 - Other complications: Gallstones, Asplenia, leg ulcer, extramedullary hematopoietic pseudotumors, hyperuricemia, & aplastic crisis secondary to folic acid deficiency, which is an uncommon complication.
- Select patients:
 1. Splenectomy → Indication: splenomegaly and Hypersplenism
 2. Potentially curative treatment
 - Allogeneic hematopoietic stem cell transplantation (Allogeneic HSCT)
 - Gene therapy: Human β-globin gene transfer (Murine β-thalassemia models)
 - IV Luspatercept (Reblozyl): a new agent, has been FDA approved for transfusion-dependent beta-thalassemia. It is a TGF-beta ligand trap that promotes erythroid maturation & reduces transfusion needs

HSCT is recommended early, before much iron deposition in organs has occurred.

in early investigational phase trials.

GLUCOSE-6-PHOSPHATE DEHYDROGENASE (G6PD) DEFICIENCY

- Definition: G6PD deficiency is a most common hereditary human enzyme defect that causes episodic hemolytic anemia because of the decreased ability of RBCs to deal with oxidative stresses. G6PD deficiency leads to excess oxidized glutathione that forces hemoglobin to denature and form precipitants called Heinz bodies. Heinz bodies cause RBC membrane damage, which leads to premature removal of these RBCs by reticuloendothelial cells within the spleen (i.e., extravascular hemolysis).
- Mode of inheritance: X-linked recessive inheritance that may affect both males and females (heterozygous) but males are therefore affected far more commonly, and more severely, than females.

ETIOLOGY

Causes of increased oxidative stress are triggers of hemolytic crisis and include:

- Consumption of Fava Bean or Broad bean (Favism)
- Drugs: antimalarial drugs (Chloroquine = possible risk, Primaquine = definite risk), sulfa drugs (Trimethoprim-sulfamethoxazole), sulfadiazine, Nitrofurantoin, Isoniazid, Dapsone, NSAIDs, ciprofloxacin, chloramphenicol, methylene blue, phenazopyridine, rasburicase, toluidine blue, pegloticase, quinine and quinolones.
- Bacterial and viral infections (most common cause): Severe enzymatic deficiency can inhibit respiratory burst activity due to reduced NADPH production in phagocytes.
- Inflammation: During an inflammatory reaction free radical are produced and can diffuse into RBCs.
- Metabolic acidosis ($\downarrow$ pH, $\downarrow$ Bicarbonate, $\downarrow$ PCO₂)

CLINICAL FEATURES

- Most patients are usually asymptomatic, without chronic hemolytic anemia or splenomegaly. Hemolysis occurs episodically due to oxidative stress on the RBCs, generated either by infection or exposure to certain drugs.
- Recurring hemolytic crises may occur, especially following triggers:
 - » Arise within 2–3 days after increased oxidative stress.
 - » Sudden onset of back or abdominal pain
 - » Jaundice, Dark urine, Transient splenomegaly.
- Recurrent severe infections causing symptoms of chronic granulomatous disease

DIAGNOSTIC APPROACH

- CBC: Hb rarely fall below 8g/dL during episodes of hemolysis, usually within normal limit.
- Peripheral blood smear: Presence of anisocytosis, abnormal forms, Heinz bodies, bite cells
 - ↳ Heinz bodies (fragments of denatured hemoglobin).
 - ↳ Blister or Bite cells: cells that appear to have had a bite taken out of their periphery, due to macrophages selectively removing the denatured hemoglobin inclusions of RBCs.
- Signs of intravascular hemolysis: Normocytic anemia, $\uparrow$ Reticulocyte count (Reticulocytosis), $\uparrow$ serum unconjugated (indirect) bilirubin, $\uparrow$ LDH, $\downarrow$ Haptoglobin and urinalysis shows: Hemoglobinuria.
- Screening test: G6PD fluorescent spot test $\rightarrow$ Negative
- Confirmatory test: Quantitative G6PD enzyme analysis (G6PD Spectrophotometry) $\rightarrow$ reduced G6PD activity
 - ↳ Specific enzyme assays for G6PD reveal a low level but may be falsely normal if they are performed during OR shortly after a hemolytic episode during the period of reticulocytosis.
 - ↳ In these cases, the enzyme assays should be repeated weeks after hemolysis has resolved.
 - ↳ In severe cases of G6PD deficiency, enzyme levels are always low.



TREATMENT OF G6PD DEFICIENCY

- Treatment:
 - » Self-limited, most patients with G6PD deficiency are asymptomatic and no treatment is required.
 - » Patient G6PD deficient must be advised to avoid known triggers (see etiology) that result in a significant oxidative challenge (E.g., certain drugs and chemicals, and some foods such as fava/broad beans).
 - » Supportive care and folic acid (vitamin B9) at dose 1-5 mg per orally (PO), once daily for 14-21 days
 - » Blood transfusions should be performed only in rare, severe cases of anemia (Hb < 7 g/dL).
- Selective advantage in areas of endemic malaria: As with sickle cell anemia, carriers of the G6PD deficiency may be less severely affected by Plasmodium falciparum malaria. Patients should be screened for G6PD deficiency before treatment with primaquine for eradication of Plasmodium vivax malaria

SICKLE CELL ANEMIA

Definition: Sickle cell anemia is an autosomal recessive disorder in which an abnormal hemoglobin leads to chronic hemolytic anemia with numerous clinical consequences. The presence of abnormal an abnormal type of hemoglobin called HbS. Results from a point mutation that causes the glutamic acid to be replaced by valine at the b6 position of the globin chain. Sickle cell anemia is the most common form of intrinsic hemolytic anemia worldwide.

CLINICAL FEATURES

1. Sickle cell trait

- Often asymptomatic
- Painless gross hematuria due to renal papillary necrosis:** often the only symptom
- Hyposthenuria:** Nocturia, Enuresis
- Recurrent urinary tract infection (UTI)
- Renal medullary carcinoma
- Very rarely, symptoms of sickle cell disease may occur as a result of severe oxygen deficiency.

2. Sickle cell disease

- Onset:** = 30% develop symptoms in the first year of life; > 90% by age 6 years, Manifests after 6 months of age as the production of HbF decreases and HbS levels increase.
- Acute symptoms**
 - Acute hemolytic crisis (severe anemia)**
 - Splenic sequestration crisis:** Splenic vaso-occlusion → entrapment and pooling of large amounts of blood in the spleen → Acute left upper quadrant pain, anemia, Reticulocytosis, and signs of intravascular volume depletion (e.g., hypotension)
 - Aplastic crisis:** Red blood cell aplasia with an acute, severe drop in hemoglobin and associated reticulocytopenia due to an infection with **parvovirus B19**. Dysmorphic erythrocytes in sickle cell disease and hereditary spherocytosis are susceptible to parvovirus B19 infection, which can temporarily suppress bone marrow erythropoiesis.
 - Hyperhemolysis:** intravascular & extravascular hemolysis triggered by mild oxygen deficiency (rare)
 - Infection**
 - Pneumonia** (Fever, fatigue, cough, sputum, chest pain, shortness of breath)
 - Meningitis** (Fever, headache, Neck rigidity, photophobia, nausea, vomiting and ASOC)
 - Osteomyelitis:** Most common cause: **Salmonella spp.**, Staphylococcus aureus
 - Sepsis:** Most common cause = Streptococcus pneumoniae
 - Vaso-occlusive events**
 - Vaso-occlusive crises (painful episodes, painful crisis):** recurrent episodes of severe deep bone pain and dactylitis → most common symptom in children and adolescents
 - Acute chest syndrome** (severe lung-related complication of sickle cell disease)
 - Priapism:** Prolonged painful erection of the penis that lasts for > 4hr & occur without sexual stimulation.
 - Stroke** (common in children)
 - Acute sickle hepatic crisis:** Manifests with RUQ pain, jaundice, nausea, fever, hepatomegaly, & ↑ LFTs
 - Infarctions of virtually any organ** (particularly spleen) & avascular necrosis with corresponding symptoms.
 - Sickle cell anemia** initially shows splenomegaly & later autosplenectomy because of hypoxia & infarction.
- Chronic symptoms:** Chronic hemolytic anemia (fatigue, weakness, pallor; usually well-tolerated), Chronic pain and Cholelithiasis (pigmented stones)
- Symptoms of other forms of sickle cell syndrome** (HbSC disease and HbS/beta-thalassemia) are similar to sickle cell anemia but less severe.

DIAGNOSTIC WORKUP

- CBC with reticulocytes count:** Mild-to-severe anemia, Elevated reticulocyte, neutrophils, and platelets.
- Peripheral blood smear:** Sickle cells/drepanocytes (crescent-shaped RBCs), Target cells, possibly Howell-jolly bodies (due to splenic dysfunction) and reticulocytosis (indicative of hemolysis)
- Iron studies:** serum iron, transferrin, ferritin levels, and serum iron-binding capacity are normal or elevated.
- Qualitative analysis:** Hb electrophoresis confirms the diagnosis and distinguishes between heterozygotes and homozygotes and other forms of sickle cell syndrome (e.g., HbSC disease) &/OR Isoelectric focusing.
- Migration towards the anode:** HbA > HbF > HbS > HbC
- On Hb electrophoresis →** Hb-S moves slowly towards Anode, Hb-A moves faster towards Anode.
- Interpretations:**



- No sickle cell trait/disease: hemoglobin A (Hb-A) and Hb-F only
- Sickle cell trait/disease: Hemoglobin S (Hb-S) is also present. Additional hemoglobin types may also be found in heterozygous sickle cell disease, e.g.: Hb-C in Hb-SC disease, Hb-D in Hb-SD, Hb-E in Hb-SE

Quantitative analysis: High performance liquid chromatography, Capillary electrophoresis

Hb reference values: HbA (Normal: 97–99%), HbS (Normal: 0%), HbA2 (Normal: 1–3%), HbF (Normal: <1%)

Interpretation	Sickle cell trait: HbA (60%), HbS (40%), HbA2 (1–2%), HbF (<2%)
	Sickle cell disease: HbA (0%), HbS (85–98%), HbA2 (1–3%), HbF (5–25%)

DNA based assay (most accurate): Replacement of both beta hemoglobin subunits with HbS is diagnostic for sickle cell anemia (HbSS); presence of 1 normal beta hemoglobin subunit and 1 HbS is diagnostic for sickle cell trait.

Reserved for prenatal diagnosis: can be done using the enzyme MstII endonuclease → Chorionic villus sampling 12 (10–12) weeks of gestation is used to estimate fetal DNA abnormality.

Radiological test: X-ray of the skull shows hair-on-end ("crew cut") sign due to periosteal reaction to erythropoietic bone marrow hyperplasia (also present in thalassemia).

TREATMENT OF SICKLE CELL ANEMIA



Prevent infections.

- Immunization: Pneumococcal vaccines, Meningococcal vaccines
- Prophylaxis with daily penicillin (at least until the age of 5 years), Alternative erythromycin
- If infection/sepsis is suspected, treat with IV 3rd generation cephalosporin (ceftriaxone) after blood culture.
 - If meningitis is also suspected: add vancomycin.
 - Second-line therapy (e.g., due to allergy): Levofloxacin, clindamycin

Prevent vaso-occlusive crises and manage anemia.

- Avoid triggers.
- First line treatment: Cap. Hydroxyurea 500mg (Hydrine, Hydra, Hydrourea) at dose 500–750 mg daily
 - Hydroxyurea increases HbF levels epigenetically and reduces the frequency of painful crises in patients whose quality of life is disrupted by frequent vaso-occlusive pain episodes (three or more per year).
 - If the response to hydroxyurea alone is not adequate than combine with erythropoietin/Blood transfusions
 - Long-term follow-up of patients taking hydroxyurea demonstrates it improves overall survival and quality of life with little evidence for secondary malignancy.
- Softgel capsule Omega-3 fatty acid supplementation (Ovaza, Omacor, One-natal, and Romega) may also reduce vaso-occlusive episodes and reduce transfusion needs in patients with sickle cell anemia.
- Tab. L-glutamine 500mg: first approved treatment for pediatric sickle cell anemia.
 - Indications: recurrent, acute complications of sickle cell disease, acute chest syndrome
- Folic acid supplementation: at dose 1mg orally daily and given transfusions for aplastic or hemolytic crises.
- ACE inhibitors: Recommended in patients with microalbuminuria.
- Cholecystectomy to treat cholelithiasis.
- Splenectomy or partial splenectomy to prevent recurrent splenic sequestration.

Management of acute sickle cell crisis

- Prompt and adequate supportive treatment: Hydration, Pain management with nonsteroidal anti-inflammatory agents (NSAIDs) and opioids, Thromboembolic prophylaxis, Nasal oxygen, Bed rest,
- Blood transfusions
- Exchange transfusions (erythrocytapheresis): Automated removal of erythrocytes containing HbS and simultaneous replacement with HbS free erythrocytes.
 - Exchange transfusions are indicated for the treatment of severe or intractable acute vaso-occlusive crises: acute chest syndrome, priapism, and stroke. Long-term transfusion therapy has been shown to be effective in reducing the risk of recurrent stroke in children. Phenotypically matched transfused RBCs are recommended to reduce the risk of RBC alloimmunization. It has been recommended that children with SS who are aged 2–16 years have annual transcranial ultrasounds and, if the Doppler velocity is abnormal (>200 cm/s or greater), the clinician should strongly consider beginning transfusions to prevent stroke.
- Iron chelation agent in patients with chronic transfusion therapy.
 - Tab. Deferasirox 400mg (Dasirox, Xefra)
 - Inj. Deferoxamine 500mg (Desferal)

Curative therapy: Allogeneic hematopoietic stem cell transplantation (Allogeneic bone marrow transplantation)

Indications: homozygotes, children < 16 years with severe disease. Curative rate > 80% CMT-2024.

DISSEMINATED INTRAVASCULAR COAGULATION (DIC)

Definition: Disseminated intravascular coagulation (DIC), Known as consumptive coagulopathy is an acquired condition marked by the activation of coagulation pathways, leading to the formation of intravascular thrombi and depletion of platelets and coagulation factors. These thrombi can cause vascular obstruction and ischemia, potentially leading to multiorgan failure. Spontaneous bleeding may occur. The presence of generalized bleeding across at least three unrelated sites is strongly indicative of DIC.

ETIOLOGY

- **Severe obstetric disorders or complications:** RPOC (Intrauterine fetus death, placental tissue), Abruptio placenta, placenta previa, HELLP syndrome, Amniotic fluid embolism, Eclampsia, Preeclampsia.
- **Traumatic:** Severe tissue injuries (polytrauma, crush injuries, burn), Head injury, Fat embolism, surgery, Acute traumatic coagulopathy, heat stroke or shock.
- **Malignancy:** Hematological malignancies such as Acute promyelocytic leukemia (APL), AML and solid tumors like pancreatic, ovarian, gastric, and non-small cell lung cancer (NSCLC) are significant contributors.
- **Severe organ destruction or failure:** severe pancreatitis, fulminant hepatitis, acute hepatic failure, liver cirrhosis, and acute respiratory distress syndrome (ARDS) signify common organ failure scenarios.
- **Vascular disorders:** Vasculitis, Aortic aneurysms, Kasabach-Merritt syndrome, or giant hemangiomas
- **Severe toxic or immunologic reactions:** Blood transfusion reaction or Acute hemolytic transfusion reaction (AHTR), organ transplant rejection (graft-versus-host disease), venomous snake bites, Adverse drug reactions
- **Sepsis or severe infections:** Viral infections, Rickettsial infections, Malaria, severe COVID-19 infection
- **Dilution-related complications:** massive bleeding, massive transfusion, and massive volume repletion/volume overload scenarios are linked to dilution.
- **Other:** Acidosis, nephritic syndrome, rhabdomyolysis, Hemolysis, New thrombus formation and dialysis.

CLINICAL FEATURES

- **History and physical exam:** depending on the underlying mechanism, identification of associated conditions such as sepsis, trauma, malignancy, obstetric complications, or severe systemic illness.
- **Clinical signs and symptoms indicative of DIC, include:**
 - **Bleeding manifestations:** Hematemesis, hematochezia, hematuria, oozing from surgical wounds or IV lines, petechiae, purpura, ecchymoses, and massive hemorrhage leading to hemoperitoneum or hemothorax.
 - **Features of organ failure:** Often stemming from hypercoagulation, leading to conditions such as microangiopathic hemolytic anemia, acute renal failure (oliguria), hepatic dysfunction (jaundice), and features of acute respiratory distress syndrome (ARDS) such as dyspnea and rales.
 - **Features of thrombotic events:** Including pulmonary thromboembolism (marked by dyspnea, chest pain, and hemoptysis), deep vein thrombosis (evidenced by lower limb edema, erythema), and neurological dysfunction, which may present as altered mental status or stroke.
 - **Severe Complications:** Such as purpura fulminans, characterized by extensive skin necrosis, and Waterhouse Friderichsen syndrome, resulting from adrenal infarcts leading to adrenal insufficiency.
 - **Signs of Shock:** Indicating compromised hemodynamics and systemic perfusion.
 - **Malignancy-related DIC** may manifest principally as thrombosis (Trousseau syndrome).

DIAGNOSTIC WORKUP

- **Coagulation profile**
 - **Prolonged aPTT,** prothrombin time (PT), bleeding time (BT), thrombin time (TT) and clotting times (CT)
 - **Decreased fibrinogen levels** (<150 mg/dL or <1.5 g/L): due to consumption and conversion to fibrin.
 - **Fibrin related markers** such as D-dimer, or fibrin degradation products (FDPs): Elevated levels (>4 times the upper limit of normal) due to ongoing fibrinolysis and breakdown of fibrin clots.
 - **Reduced level of coagulation factors:** Factor V, factor VIII, factor X and factor XIII
- **Complete blood count (CBC):** Decreased platelet count (<100 x 10⁹/L) due to consumptive coagulopathy.
- **Peripheral blood smears:** Evidence of schistocytes (fragmented red blood cells) indicative microangiopathic hemolytic anemia associated with Disseminated intravascular coagulation (DIC).
- **Calculate ISTH DIC score.**

- Consider additional tests based on clinical presentation and underlying conditions:
- » **LFTs:** to assess liver function and to detect any dysfunction or damage.
 - » **BUN and Creatinine:** to evaluate kidney function. Elevated in AKI.
 - » **Serum electrolytes:** Determine the balance of electrolytes.
 - » **Serum lactate:** to assess tissue perfusion and oxygenation, particularly in cases of shock or tissue hypoxia.
 - » **ABGs:** to assess respiratory failure or metabolic acidosis.
 - » **Specialized Tests:** should be considered on a case-by-case basis in consultation with a specialist or hematologist.
 - » **Monitoring Treatment:** Anti-Xa activity can assess the anticoagulant effect of heparin therapy.
 - » **DIC Subtype Classification:** The following test are useful when subtype uncertainty exists such as soluble fibrin, Thrombin-Antithrombin Complex (TAT), Plasminogen Activator Inhibitor-1 (PAI-1), Plasmin-Plasmin Inhibitor Complex (PPIC) and Coagulation Inhibitors (Decreased protein C and antithrombin levels).
 - » **Radiological tests:** Dependent on the underlying disorder and areas of thrombosis and hemorrhage.

INTERNATIONAL SOCIETY OF THROMBOSIS AND HAEMOSTASIS (ISTH) DIC SCORE/ALGORITHM

1. PRESENCE OF AN UNDERLYING DISORDER KNOWN TO BE ASSOCIATED WITH DIC?

- » If YES: **proceed.**
- » If NO: do not use this algorithm/ISTH DIC score.

	RESULTS	POINTS
2. COAGULATION PROFILE TEST		
A. Platelet count	> 100,000/ μ L (10^9 /L)	0
	50,000–100,000/ μ L (10^9 /L)	1
	< 50,000/ μ L (10^9 /L)	2
B. Increase level of Fibrin related markers such as D-dimer, soluble fibrin, fibrin degradation products (FDPs)	No increase	0
	Moderate increase	2
	Strong increase	3
C. Prolonged prothrombin time (PT)	< 3 seconds	0
	3 – 6 seconds	1
	> 6 seconds	2
D. Fibrinogen level	> 100 mg/dL (> 1.0 g/L)	0
	< 100 mg/dL (< 1.0 g/L)	1

3. INTERPRETATION OF ALGORITHM

- » Score of 5 or higher: Compatible with acute DIC (Overt DIC likely) → repeat coagulation profile daily.
- » Score < 5: Possible latent DIC (non-overt DIC) → repeat coagulation profile within next 1-2 days.



TREATMENT OF DISSEMINATED INTRAVASCULAR COAGULATION (DIC)

- Treatment of underlying causative disorder**
 - » Early identification & prompt treatment of the underlying condition or disorders known to precipitate DIC.
 - » **Sepsis:** Aggressively manage sepsis with appropriate antibiotics and source control – See sepsis
 - » Address trauma-related injuries promptly.
- Supportive Care:**
 - » Provide organ support as needed, including respiratory support, hemodynamic stabilization, and renal replacement therapy for acute kidney injury (AKI) and management of shock.
 - » Maintain adequate tissue perfusion and oxygenation.
 - » Monitor and manage fluid and electrolyte imbalances.
 - » Initiate clinical and serial laboratory monitoring to assess the patient's response to treatment.
 - » Avoid invasive procedures (intravenous catheters or incisions), if possible.
 - » **Patient with Vitamin-K deficiency:** Inj. Vitamin-K 10mg IV, once
 - » Monitoring of laboratory parameters such as platelets, aPTT, PT, fibrinogen every 4–12 hours as clinically indicated until DIC resolves.
- Administration of Blood products:** The decision to administer blood products should primarily depend on the presence or risk of bleeding, with laboratory parameters serving as a treatment guide rather than the sole basis for transfusion. Early involvement of specialists is crucial. Blood-borne diseases of all types (hepatitis, HIV) and febrile reactions are always a risk in giving human blood products.

- » **Packed Red Blood Cells (pRBCs) transfusion:** Indicated in Active bleeding or $Hb \leq 7$ g/dL. Goal hemoglobin (Hb) > 8 g/dL or improvement in symptomatic anemia
- » **Platelets transfusion:** Indicated in Active bleeding or high risk of bleeding (e.g., planned invasive procedure) with platelet count $< 50,000 \times 10^9/L$. No bleeding with platelet count $< 10,000-20,000 \times 10^9/L$. Goals: Active bleeding or high risk of bleeding: platelet count $> 20-50,000 \times 10^9/L$ and During massive transfusion (intracranial hemorrhage) platelet count $> 50,000 \times 10^9/L$.
- » **Fresh Frozen Plasma (FFP):** Administered when PT or aPTT is more than 1.5 times the normal value in bleeding patients or those undergoing invasive procedures. Consider for bleeding cases with fibrinogen levels < 150 mg/dL and as part of a massive transfusion protocol. Goals: PT and aPTT $< 1.5 \times$ normal and fibrinogen levels $> 100-150$ mg/dL.
- » **Cryoprecipitate:** Administered in cases of bleeding with fibrinogen levels < 150 mg/dL despite FFP transfusion or when FFP transfusion is not feasible. Goals: fibrinogen level $> 100-150$ mg/dL
- » **Prothrombin Complex Concentrate (PCC):** Decision to administer in patients with active bleeding when FFP transfusion is not feasible (e.g., due to volume overload).
- Cautions:** May only partially correct coagulopathy. May alter the procoagulant-anticoagulant balance towards thrombosis. Monitoring of antithrombin activity and protein C levels is advised.
- 4. **Antifibrinolytic Therapy:** should be used with extreme caution because they inhibit the fibrinolytic pathways, which may worsen the symptoms and signs of thrombosis. They are occasionally used in patients with severe refractory bleeding resistant to conventional replacement therapy or in patients with hyperfibrinolysis associated with acute promyelocytic leukemia and other forms of cancer.
 - » **Inj. Tranexamic acid 500mg/5ml (Transamin) x** at dose 1g IV every 8 hours. Not routinely recommended.
 - ↳ Indicated in patients with severe bleeding and hyperfibrinolysis, particularly post-trauma. Administer promptly if indicated.
 - ↳ **Contraindications:** Avoid in patients with nonsymptomatic or organ failure type DIC. Also contraindicated in APL patients undergoing ATRA treatment.
 - » **Aminocaproic acid** is generally contraindicated in DIC.
- 5. **Anticoagulation therapy**
 1. **Prophylactic heparin:** Used for DVT prophylaxis in critically ill patients without bleeding.
 - » **LMWH: Inj. Enoxaparin 40mg/0.4ml (Clexane)** at dose 40 mg x subcutaneous (SQ), once daily
 - » **OR Inj. Unfractionated heparin (UFH)** at dose 5,000 units SQ every 8-12 hours
 2. **Therapeutic heparin:** indicated for clinically overt thromboembolic events.
 - » **LMWH: Inj. Enoxaparin 60mg/0.6ml OR 80mg/0.8ml (Clexane)** at dose 1mg/kg subcutaneous (SQ), twice daily (BD), sometimes preferred over Inj. Unfractionated heparin (UFH)
 - » **OR Inj. Unfractionated heparin (UFH)** at dose 80 units/kg IV bolus, then 18 units/kg/hour infusion with aPTT monitoring; follow local protocols for dose adjustment. Consider in high bleeding risk patients due to its short half-life and reversibility.
 3. **Advance options of coagulation inhibitors:** Consider in individual cases with consultation of a specialist.
 - » **Antithrombin (AT):** Not routinely recommended due to a lack of supporting evidence.
 - » Plasma-derived activated protein-C (APC).
 - » Recombinant human thrombomodulin (rhTM).
 - » Synthetic inhibitors of serine proteases.

RECOMMENDATIONS OF TREATMENT BY TYPE OF DIC

1. **Nonsymptomatic type DIC:** Administration of Platelets &/or FFP (if required), and prophylactic heparin. Antifibrinolytic therapy (tranexamic acid) and Fibrinolytic therapy are generally discouraged.
2. **Organ failure type DIC:** Consider therapeutic heparin and advanced treatments options. Antifibrinolytic therapy and Fibrinolytic therapy (streptokinase and alteplase) are generally discouraged.
3. **Bleeding type DIC:** Administer of **Packed Red Blood Cells (pRBCs)**. Antifibrinolytic therapy (individual decision), also Consider advanced treatments options.
4. **Massive bleeding type DIC:** administration of Blood products such as **Packed Red Blood Cells (pRBCs)**, Platelets, FFP and Cryoprecipitate. Consider Antifibrinolytic therapy (individual decision) and advanced treatments options. Anticoagulation and Fibrinolytic therapy are generally discouraged.

OSTEOPOROSIS

ETIOLOGY & RISK FACTORS

Primary osteoporosis (most common)

Type I (postmenopausal osteoporosis):

Post-menopausal women

- » Estrogen stimulates osteoblasts & inhibits osteoclasts.
- » The decreased estrogen levels following menopause lead to increased bone resorption.

Type II (senile osteoporosis): gradual loss of bone mass as patients ages (especially > 70 years)

Idiopathic osteoporosis

- » Idiopathic juvenile osteoporosis
- » Idiopathic osteoporosis in young adults

Additional risk factors

- » Excessive alcohol consumption
- » Cigarette smoking
- » Immobilization or poor physical activity
- » Malabsorption syndrome (e.g., celiac disease)
- » **Malnutrition:**
 - » Poor calcium intake
 - » vitamin-D deficiency)
- » Anorexia and Low body weight
- » Family history of osteoporosis
- » Personal history of fracture

Clinical features

- » Mostly patients are typically asymptomatic until fractured has occurred
- » **Fragility fractures:** pathological fractures that are caused by Every day-activities (bending over, sneezing) or minor trauma (falling from standing height)
- » **Common sites of major osteoporotic fractures:** vertebral (most common) > femoral neck > distal radius (Colles's fracture) > other long bones (e.g., humerus)
- » Low back pain which radiates around the trunk or down the limb
- » A gradual loss of height and appearance of thoracic kyphosis
- » Difficulty in bearing weight

Diagnostic workup

- » Complete blood count (CBC), Albumin, Complete Metabolic Panel (CMP), BUN, Creatinine, Electrolytes
- » Serum PTH, calcium, phosphorus, and alkaline phosphatase usually normal
- » Serum 25-Hydroxyvitamin-D: Low

Secondary osteoporosis» Drug-induced/iatrogenic

- » Most commonly due to systemic long-term therapy with corticosteroids (for example in patients with autoimmune disease)

» Long-term therapy involving:

- **Anticonvulsants:** Phenytoin, Carbamazepine
- Levothyroxine
- SGLT2 inhibitors & Pioglitazone
- **Antipsychotic:** Lithium
- **Anticoagulants:** Heparin, Warfarin
- **PPIs:** Omeprazole, Esomeprazole etc.
- **Aromatase inhibitors:** Nastrozole, Letrozole
- **Immunosuppressants:** Cyclosporine, Tacrolimus
- Androgen deprivation therapy (ADT)

» Endocrine/metabolic:

- » Hyperparathyroidism
- » Hyperthyroidism/thyrotoxicosis
- » Hypercortisolism
- » Hypogonadism
- » Renal disease

» Malignancy: Multiple myeloma

Rx

1. **Inj. Cholechalceferol** (Indrop-D, Miura-D)
ایک انجکشن ایک کپ دودھ یا پانی میں صبح نہار منہ
Once weekly or 2 weekly give as per vitamin D³ level
2. **Tab. Diclofenac potassium** (Cafiam, Dyclo-P)
OR **Tab. Naproxen sodium 500mg** (Flexin, Neoprox)
1 – 0 – 1 (Twice daily)
3. **Tab. Calcium & vitamin-D** (Calone-D, Osteocare)
0 – 0 – 1 (OD)
4. **Tab. Alendronate sodium 70mg** (Fosamax, Drat, Firmofos)
Once weekly x 40 minutes before breakfast
OR **Tab. Risedronate sodium** (Atconate, Actonel, Risonate)
Dose: 35mg = Once weekly or 150mg = Once monthly
Must be taken at morning with plain water at least 40 minutes before breakfast, the patient must remain up right after taking the drug to reduce the risk of esophagitis.
ہفتے میں ایک گولی صبح نہار منہ

» Additional test to rule out specific causes:

- Celiac antibodies
- TSH
- Myeloma screen: protein electrophoresis

Radiological test: X-ray, CT scan, MRI

Gold standard test: DEXA Scan (Dual-Energy X-ray Absorptiometry)

- » DEXA measures bone mineral density (BMD); at the lumbar spine and hip/femoral neck using two x-ray beams.
- » The diagnosis is confirmed if any of the following diagnostic criteria for osteoporosis are fulfilled.
 - T-score ≤ -2.5 standard deviations (SDs) on Dual-Energy X-ray Absorptiometry (DEXA)
 - T-score -1 to -2.5 SD in patients at increased risk of major osteoporotic fracture.
 - History of a major osteoporotic fragility fracture (regardless of BMD).

Rx

1. Inj. Cholechalceferol (Indrop-D/Miura-D)
ایک انجکشن ایک کپ دودھ یا پانی میں صبح نہار منہ
Once weekly/2 weekly give as per vitamin D³ level
2. Tab. Naproxen sodium 500mg (Flexin, Neoprox)
1-0-1 (Twice daily)
3. Tab. Qalsan-D
0-0-1 (OD)
4. Cap. Esomeprazole 40mg (Nexum, Esso)
0-0-1 (OD)
کھانے سے 30 منٹ پہلے
5. Tab. Alendronate sodium (Drat)
Once weekly on empty stomach
ہفتے میں ایک گولی صبح نہار منہ

POST-MENOPAUSAL OSTEOPOROSIS

△
c/c:

Postmenopausal osteoporosis
Postmenopausal women →
Estrogen stimulates osteoblasts and inhibits osteoclasts.
The decreased estrogen levels following menopause lead to increased bone resorption

Rx

1. Inj. Cholechalceferol (Indrop-D, Miura-D)
ایک انجکشن ایک کپ دودھ یا پانی میں صبح نہار منہ
Once weekly/2 weekly give acc. Serum vit. D³ level
2. Tab. Diclofenac potassium 50mg (Caflam, Dyclo-P)
OR Tab. Aceclofenac 100mg (Acenac, Acelo)
OR Tab. Lornoxicam 8mg (Xikarapid, Atcam)
1-0-1 (Twice daily)
3. Tab. Calcium & vitamin-D (Calone-D, Osteocare)
0-0-1 (Once daily)
4. Tab. Vonoprazan 20mg (Vocinti, Vonozan)
0-0-1 (OD)
5. Tab. Ibandronate acid 150mg (Bonviva, Adronil, Ibnate)
Once weekly on empty stomach
ہفتے میں ایک گولی صبح نہار منہ

ARTHRITIS

△ ARTHRITIS

c/c:

- Pain.
- Stiffness.
- Swelling.
- Redness.
- Decreased range of motion.

Rx

Prescription #1

1. Tab. Diclofenac Potassium 50mg (Caflam, Maxit, Dyclo-P)
OR Tab. Aceclofenac 100mg (Acenac, Acemed, Alkeris)
OR Cap. Piroxicam 20mg (Feldine, P-cam, Paxil)
1-0-1 (Twice daily)
2. Tab. Glucosamine Sulfate + Chondroitin (Cartigen, Gevolox Plus, Jovit)
1-0-1 (Twice daily)
3. Cap. Omeprazole 40mg (Risek, Ruling)
0-0-1 (OD)
کھاتے سے 30 منٹ پہلے

Rx

Prescription #2

1. Tab. Lornoxicam 4mg or 8mg (Xikarapid, Atcam)
OR Tab. Meloxicam 7.5mg or 15mg (Melfix, Xobix, Mits)
OR Tab. Piroxicam + B-Cyclodextrin (Brexin, Briax, Pirexen)
1-0-1 (Twice daily)
2. Syp. Glucosamine Sulfate + Chondroitin + Hyaluronic acid (Ossis)
10ml-0-10ml (10ml x Twice daily)
3. Cap. Esomeprazole 40mg (Eskem, Nexum, Esso)
0-0-1 (OD)
کھاتے سے 30 منٹ پہلے

POST CHIKENGUNYA ARTHRITIS

△
c/c:

- Fever (sometimes as high as 104 °F)
- Joint pain
- Headache
- Muscle pain
- Rash
- Swelling around the joints
- Less commonly, symptoms can be accompanied by a:
 - Maculopapular rash (similar to measles or heat rash),
 - Conjunctivitis
 - Nausea, and vomiting.

Rx

1. Tab. Paracetamol 325mg + Tramadol 37.5mg (Tonoflex-P, Pentra Plus)
1-0-1 x orally twice daily (BD)
OR Tab. Meloxicam 15mg (Mobix, Melfix)
OR Tab. Lornoxicam 8mg (Xikarapid, Atcam)
0-0-1 x orally once daily (OD)
2. Tab. Dexamethasone (Oradexon, Kanadex)
2-0-2 (2 tablets x BD) then tapered down
OR Tab. Methotrexate (MTX) 2.5mg (Cytotrexate, Unitrexate)
Dose: 3 tablets of MTX = 7.5mg Once weekly
OR Tab. Hydroxychloroquine 200mg (HCQ) x OD
3. Cap. Omeprazole 40mg (Omega, Risek, Ruling)
OR Cap. Esomeprazole 40mg (Eskem, Nexum, Esso)
0-0-1 (OD)
کھاتے سے 30 منٹ پہلے

OSTEOARTHRITIS

Clinical features

Common clinical findings

- ☞ Pain during or after exertion (e.g., at the end of the day) that is relieved with rest, commonly involves the hands, hips, and knees joint
- ☞ Pain in both complete flexion and extension
- ☞ Crepitus on joint movement
- ☞ Joint stiffness and restricted/decrease range of motion
- ☞ Morning joint stiffness usually lasting < 30 minutes
- ☞ Possible formation of varus deformity if the knee is affected
- ☞ Joints are usually asymmetrically involved, as opposed to rheumatoid arthritis.
- ☞ **Findings in late-stage disease:** constant pain (including at night) and a more severely restricted range of motion than during the early stages

Joint-specific findings on physical examination

- ☞ **Heberden nodes:** Pain and nodular thickening (swelling) on the dorsal sides of the DIP joints
Note: In contrast to rheumatoid arthritis, osteoarthritis can affect the distal interphalangeal (DIP) joints.
- ☞ **Bouchard nodes:** Pain and nodular thickening on the dorsal sides of the proximal interphalangeal joints
- ☞ **Rhizarthrosis:** Osteoarthritis of the 1st carpometacarpal joint, between the trapezium & 1st metacarpal bone
- ☞ **Hallux rigidus:** Osteoarthritis of the first metatarsophalangeal joint, between the first metatarsal and the first proximal phalanx; characterized by hypertrophy of the sesamoid bones

Diagnostic workup

- » **CBC:** normal or may show iron deficiency anemia due to excessive use of NSAIDs
- » **ESR & CRP are usually normal**
- » **X-ray of affected joints:** May reveal narrowing of the joint space; osteophyte formation and lipping of marginal bone; and thickened, dense subchondral bone. Bone cysts may also be present.
- » **Arthrocentesis:** Synovial fluid analysis usually doesn't show the presence of inflammation (WBC < 2000 mm³).
- » **Arthroscopy:** may show a thickened capsule, synovial hypertrophy, and/or ulcerated cartilage

Heberden's node Bouchard's node



Heberden nodes at the DIP joints.
There is some swelling beginning at the proximal interphalangeal joints creating Bouchard nodes.

Rx

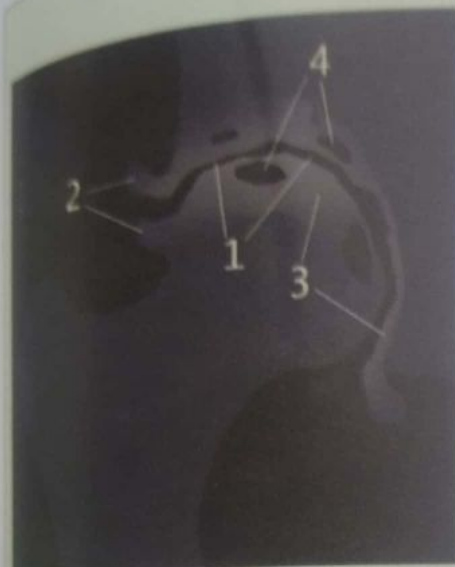
Prescription #1

General treatment

- ☞ Weight loss
- ☞ Regular exercise
- ☞ Targeted muscle growth, physiotherapy, and medical training therapy
- ☞ Topical and heat therapy

1. **Cap. Celecoxib 100mg OR 200mg** (Celbexx, Seleco)
OR **Tab. Diclofenac potassium 50mg** (Caflam, Dyclo-P)
1-0-1 (Twice daily)
(Cartigen, Gevolox Plus, Jovit)
2. **Tab Glucosamine Sulfate + Chondroitin**
1-0-1 (Twice daily)
3. **Cap. Omeprazole 40mg** (Omega, Ruling, Risek)
OR **Cap. Esomeprazole 40mg** (Eskem, Eso, Nexum)
0-0-1 (OD)

کھانے سے 30 منٹ پہلے



Radiological signs of osteoarthritis

1. Irregular joint space narrowing
2. Subchondral sclerosis
3. Osteophytes (also: bone spurs)
4. Subchondral cysts



X-Ray of knee AP view

Marked lateral compartment narrowing (indicated by white lines and arrows) is accompanied by subchondral sclerosis (green overlay) and osteophyte formation (red overlay). Tibial spine osteophytes (example indicated by yellow overlay) are also visible.

Rx

Prescription #2

1. **General:** Exercise, weight loss, and Physiotherapy
2. **Tab. Paracetamol + Tramadol** (Tonoflex-P, Distalgesic)
OR **Tab. Meloxicam 15mg** (Mobix, Melfix)
OR **Tab. Lornoxicam 8mg** (Xikarapid, Atcam)
1-0-1 (Twice daily)
(Cartigen, Gevolox Plus, Jovit)
3. **Tab. Glucosamine Sulfate + Chondroitin**
1-0-1 (Twice daily)
4. **Cap. Esomeprazole 40mg** (Nexum, Esso)
1-0-0 (OD)
کھاتے سے 30 منٹ پہلے

Rx

Prescription #3

1. **General:** Exercise, weight loss, and Physiotherapy
2. **Cap. Duloxetine 30mg, or 60mg** (Dulan, Lyta, Cymbalta)
0-0-1 (Once daily), may increase up to 60mg/day
(Cartigen, Gevolox Plus, Jovit)
3. **Tab Glucosamine Sulfate + Chondroitin**
1-0-1 (Twice daily)
4. **Topical Diclofenac 1% gel** (Voltral gel, Dicloran gel)
Apply topically on affected joint 3-4 time per day
5. **Cap. Esomeprazole 40mg** (Nexum, Esso)
0-0-1 (OD)
کھاتے سے 30 منٹ پہلے

Intra-articular injections

- ☞ Intra-articular injections of corticosteroids, hyaluronate, or platelet-rich plasma have not convincingly produced long-term benefits in reducing pain or preserving function in osteoarthritis.
- ☞ A 2-year controlled trial demonstrated that injecting the knee with triamcinolone every 12 weeks was no more effective than injecting saline in reducing knee pain and resulted in more cartilage volume loss.
- ☞ Similarly, platelet-rich plasma injections were no better than saline injections in improving knee pain or slowing disease progression in a randomized, controlled trial of patients with knee osteoarthritis.

Interventional therapy

- » **In severe courses:** intraarticular glucocorticoid injections (not a long-term treatment!) - Inj Kanacort-A 40mg/ml
- » **Surgical therapy:** if conservative and interventional measures fail
- » **Endoprosthesis** (joint replacement)

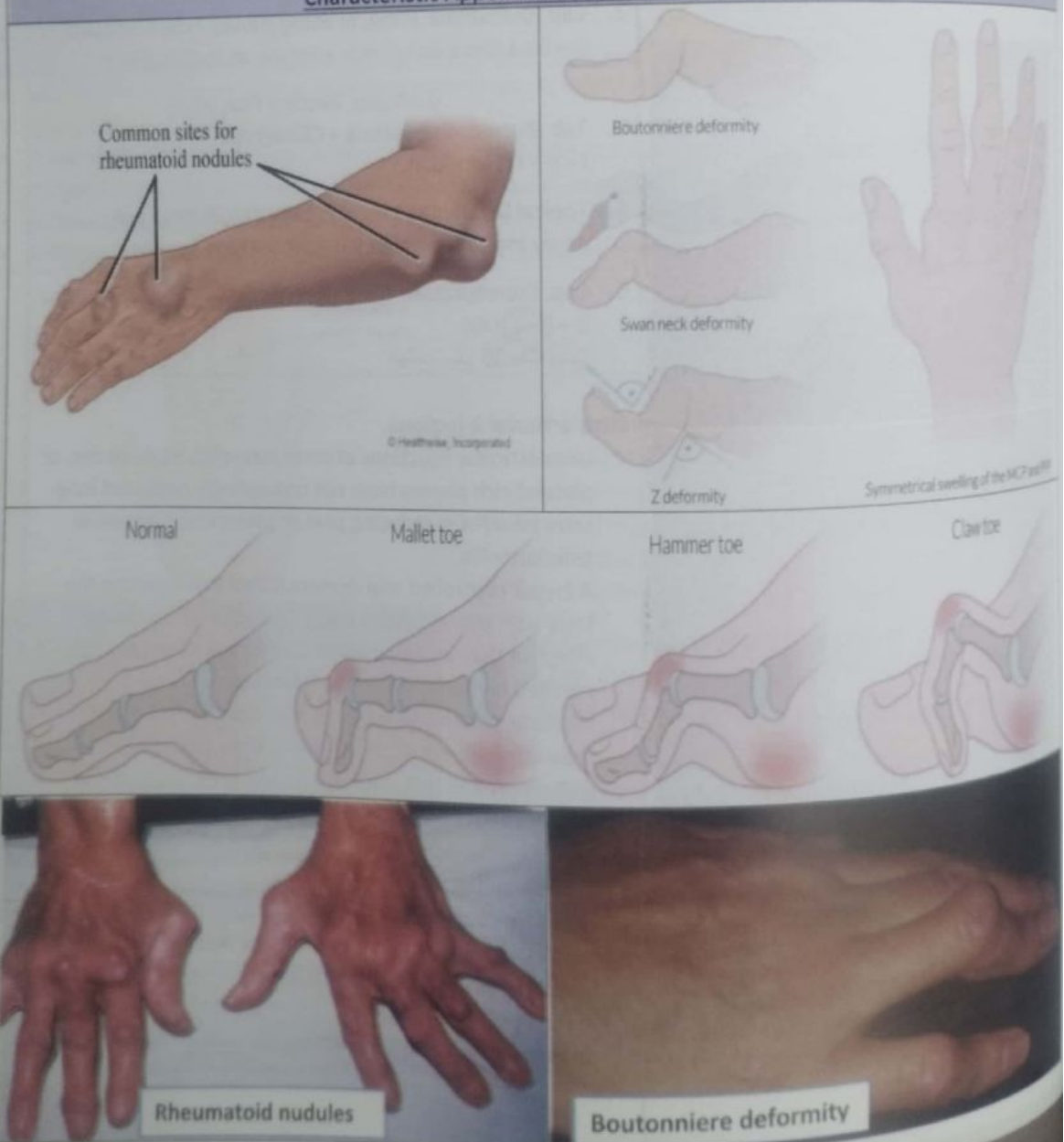
X-ray of both knees joint - Osteoarthritis



X-Ray knees (AP standing view)

Marked bilateral medial compartment joint space narrowing is accompanied by surface irregularity (indicated by red lines), subchondral sclerosis (example indicated by green overlay), and prominent osteophytes (examples indicated by arrowheads). Subluxation of the medial femoral condyles is also seen (indicated by dashed arrows). The lateral compartments show only mild degenerative changes.

Characteristic Appearance of Rheumatoid arthritis



RHEUMATOID ARTHRITIS

Rheumatoid arthritis (RA) is a common form of inflammatory arthritis, occurring throughout the world and in all ethnic groups. The prevalence of RA is approximately 0.8%–1.0% in Europe and South Asia, with a female-to-male ratio of 3:1 (female > male and peak incidence: > 65 years) and lower in South-east Asia (0.4%).

Clinical features

ARTICULAR FEATURES

- Polyarthralgia
 - Symmetrical pain and swelling of affected joints (also at rest)
 - Mostly affected joints: Metacarpophalangeal (MCP) joints, Proximal interphalangeal (PIP) joints and Wrist joints and Knee joints
- Morning joint stiffness: often > 30 minutes, that usually improves with activity.
- Joint deformities:
 - Rheumatoid hand is characteristic and typically manifests with one or more of the following deformities:
 1. Deepening of the interosseous spaces of the dorsum of hand
 2. Swan neck deformity: PIP hyperextension and DIP flexion
 3. Boutonniere deformity: PIP flexion and DIP hyperextension.
 4. Hitchhiker thumb deformity (Z deformity of the thumb): hyperextension of the interphalangeal joint with fixed flexion of the MCP joint
 5. Ulnar deviation of the fingers
 6. Piano key sign: dorsal subluxation of the ulna
 - Hammer toe or claw toe
 - Atlantoaxial subluxation

EXTRA-ARTICULAR FEATURES

- Constitutional symptoms: Low-grade fever, Myalgia, Malaise, Fatigue, Weight loss and Night sweats
- Skin subcutaneous rheumatoid nodules: Nontender, firm, subcutaneous swellings (2 mm–5 cm) → Commonly occur in areas exposed to higher pressure, e.g., extensor side of the forearm, bony prominences
- Lungs: interstitial lung disease (ILD), Pleuritis, pleural effusions.
- Eye: scleritis, episcleritis, scleromalacia and keratoconjunctivitis sicca
- Endocrine: secondary sjogren syndrome
- Blood: Anemia of chronic disease, Splenomegaly (seen in 5%; only 1% have Felty's syndrome: Rheumatoid arthritis + splenomegaly + neutropenia, Large granular lymphocyte leukemia, Lymphoma)
- Musculoskeletal: Tenosynovitis & bursitis, Carpal tunnel syndrome and Tarsal tunnel syndrome
- Heart: Pericarditis and myocarditis, increased risk of myocardial infarction, stroke, CHF, and atrial fibrillation.
- Vascular: Peripheral vasculitis, manifests as livedo reticularis, Raynaud phenomenon, Purpura, Vasculitic ulcers, Necrotizing fingertips and Peripheral neuropathy
- Neuropsychiatric: Depression

Diagnostic workup

- CBC: may show anemia of chronic disease, thrombocytosis
- Acute inflammatory markers/Acute phase reactants: ↑ CRP & ESR
- TSH & thyroid antibodies: to rule out an autoimmune thyroid disease, which is common in patients with RA
- Elevated Antinuclear antibodies (ANA) → in 30–50% of patients with RA
- Specific test for Rheumatoid arthritis
 - ↳ Anti-CCP (Anticyclic citrullinated peptide): highly specific > 90%
 - ↳ Rheumatoid factor (RF): IgM auto-antibodies against the Fc region of IgG antibodies
- Synovial fluid analysis: Fluid is collected by joint aspiration. Not routinely recommended.
- Initial radiological test: X-ray of the affected joint [i.e. both hands (dorsopalmar view) and feet]
 - ↳ Early: soft tissue swelling, osteopenia (juxta-articular)
 - ↳ Late: joint space narrowing, marginal erosions of cartilage and bone, osteopenia, subchondral cysts
- High-resolution ultrasound of affected joint: joint effusion, formation of pannus.
- MRI of affected joint: Can help detect early changes in large joints (e.g., subclinical synovitis). Consider especially if cervical spine involvement is suspected.
- Radiological imaging for suspected extra-articular features: CT chest for ILD, ECG & Echo for pericarditis.



CRITERIA FOR DIAGNOSIS OF RHEUMATOID ARTHRITIS

	Criterion	Points
Joints affected	» 1 large joint	0
	» 2–10 large joints	1
	» 1–3 small joints	2
	» 4–10 small joints	3
	» > 10 joints (at least 1 small joint)	5
Serology	» Negative RF and ACPA	0
	» Low positive RF or ACPA	2
	» High positive RF or ACPA	3
Duration of symptoms	» Less than 6 weeks	0
	» More than 6 weeks	1
Acute phase reactants	» Normal CRP and ESR	0
	» Abnormal CRP or ESR	1

Interpretation: Patients with a score ≥ 6 are considered to have definite rheumatoid arthritis.

MANAGEMENT GUIDELINES OF RHEUMATOID ARTHRITIS

1. General measure

- » Refer early to a rheumatologist.
- » Disease activity is measured using the **DAS28 score**
- » **Treatment should be escalated until satisfactory control is achieved: 'treat to target'**
 - ↳ **Target at 3 months:** $\geq 50\%$ improvement in the disease activity index
 - ↳ **Target at 6 months:** low disease activity (or remission)
 - ↳ **Targets not reached:** Consult rheumatology to adjust treatment.
- » **Education and counselling of all patients**
- » Physiotherapy e.g. exercise, joint protection
- » Occupational therapy e.g. Adaptations, aids, Splints
- » Podiatry and chiropody e.g. Orthotics, surgical shoes
- » Pain control, disease control and psychotherapy
- » Heat or cold packs for pain management.
- » ASCVD prevention measures are associated with improved outcomes in rheumatoid arthritis patients
- » Smoking cessation: Smoking also increases symptoms of rheumatoid arthritis

2. Non-steroidal anti-inflammatory drugs (NSAIDs) and selective COX-2: They are good for symptom relief but do not prevent erosions or alter disease progression. They are not appropriate for monotherapy and should only be used in conjunction with DMARDs, if at all. Paracetamol and weak opiates are not effective.

- » **Tab. Diclofenac sodium 50mg** (Voren, Voltral) x at dose 50mg orally every 8-12 hourly (TDS/BD)
- » **OR Tab. Naproxen sodium 250mg or 500mg** (Flexin, Neoprox) x at dose 250-500mg orally twice daily
- » **OR Tab. Meloxicam 7.5mg OR 15mg** (Xobix, Melfix) at dose 7.5 to 15mg orally once daily
- » **OR Tab. Lornoxicam 4mg OR 8mg** (Acabel) at dose 4-8mg orally once daily
- » **OR Cap. Celecoxib 100mg OR 200mg** (Celbexx, Celebrex) at dose 100-200mg orally twice daily (BD)
- » **OR Tab. Etoricoxib 60mg OR 90mg** (Flexia, Etoxi) at dose 60-90mg orally once daily (OD)

3. Short term low-dose corticosteroids: Tab. Prednisolone 5mg (Deltacortril) at dose 5-10mg orally once daily

- » Produce a prompt anti-inflammatory effect and slow the rate of articular erosion.
- » **Low-dose corticosteroids are often used as a "bridge" to reduce disease activity until the slower acting DMARDs take effect and should be used for < 3 months.** Longer-term corticosteroids are used only in patients with highly active disease who do not respond to maximum doses of DMARDs.
- » Higher doses are used to treat serious extra-articular features (e.g., pericarditis, necrotizing scleritis)
- » **Intra-articular corticosteroids (triamcinolone)** may be helpful for symptom control if one or two joints are the chief source of difficulty. **Inj. triamcinolone at dose 10-40mg x Intra-articularly;** OR 40-120mg x IM, depending on the size of the joint to be injected, may be given but not more than four times a year to prevent cartilage loss.
- » **All patients receiving long-term corticosteroid therapy should take measures to prevent osteoporosis**
- » Steroids should be tapered gradually discontinued, within 3-4 months as per disease response.

4. Conventional DMARDs:

• **First-line and DMARD of choice for patients with rheumatoid arthritis: Methotrexate (MTX)** at dose 7.5mg or 10mg orally once weekly. If the patient has tolerated methotrexate but has not responded in 1 month, the dose can be increased to 15 mg orally weekly. The maximal oral dose is usually 20-25mg orally weekly. Before starting MTX, check CBC, LFTs and Renal function, monitoring should be done every three months. To minimize side effects in All patients should be prescribed either daily folic acid 1-5mg OR weekly leucovorin calcium (2.5-5 mg taken orally 24 hours after the dose of methotrexate) to reduce gastric irritation, stomatitis, cytopenias, and hepatotoxicity. Do not give NSAIDs on the same day as Methotrexate, as they can worsen the side effects of Methotrexate by inhibiting its renal excretion. Contraindications to MTX include preexisting liver disease, infection with hepatitis B or C, ongoing alcohol use, and renal impairment (creatinine clearance <30 mL/minute) and in pregnancy

• **Sulfasalazine** at dose 500 mg orally twice daily and then increased each week by 500 mg until the patient improves or the daily dose reaches 3000 mg. This drug is often used in combination with methotrexate when methotrexate alone does not adequately control disease activity. Consider in patients with low disease activity if **Methotrexate (MTX)** is contraindicated, e.g., during pregnancy.

Side effects: Diarrhea, Agranulocytosis/neutropenia, thrombocytopenia, cutaneous HSR, it is also causing hemolysis in patients with G6PD deficiency, so a G6PD level should be checked before initiation

Monitoring should be done with CBC every 2-4 weeks for the first 3 months, then every 3 months

• **Hydroxychloroquine (HCQ)** at dose 200-400 mg/day orally (not to exceed 5 mg/kg/day). Monotherapy with hydroxychloroquine (HCQ) should be reserved for patients with very mild disease because only a small percentage will respond and often only after 3-6 months of therapy. hydroxychloroquine (HCQ) is often used in combination with Methotrexate (MXT) and sulfasalazine (so-called "triple therapy").

• **Leflunomide** at dose 20mg orally daily as a single dose. Alternative to Methotrexate. Consider if all other conventional DMARDs are contraindicated. The most frequent side effects are diarrhea, rash, reversible alopecia, and hepatotoxicity. Some patients experience dramatic unexplained weight loss. The drug is teratogenic and has a half-life of 2 weeks, but active metabolites can be detected for up to 2 years. Thus, it is contraindicated in premenopausal women who wish to bear children.

• **JAK inhibitors (Tofacitinib, baricitinib):** they are used to manage severe RA that is refractory to methotrexate or other agents. JAK inhibitors are oral agents that can be used either as monotherapy or in combination with methotrexate. **Side effects:** Severe infections, TB reactivation, Anemia.

1. Tab. Tofacitinib at dose 5mg orally twice daily

2. OR Tab. Baricitinib at dose 2 mg or 4 mg orally once daily

3. OR Tab. Upadacitinib at dose 15mg orally once daily.

5. Biologic DMARDs: Indicated in persistent moderate or severe disease rheumatoid arthritis after 3 months of conventional DMARD therapy.

• **Tumor Necrosis Factor (TNF) Inhibitors:**

• **Etanercept:** 50 mg subcutaneously once weekly or 25 mg twice weekly

• **Adalimumab:** 40 mg subcutaneously every other week

• **Infliximab:** at dose 3-10 mg/kg intravenously; infusions are repeated after 2, 6, 10, and 14 weeks and then are administered every 8 weeks.

• **Non-TNF Biologics:**

• **Rituximab:** 1000 mg intravenously on days 1 and 15, repeated every 6-12 months

• **Abatacept:** 10 mg/kg intravenously at 0, 2, and 4 weeks, then every 4 weeks

6. **Combination DMARDs:** Generally, DMARDs have greater efficacy when administered in combination than when used individually. The most used combination is methotrexate with a TNF inhibitor. Still, most patients who require DMARD therapy are given methotrexate monotherapy initially because this regimen is effective in up to one-third of patients and is less expensive and less toxic than combination therapy. The combination of methotrexate, sulfasalazine, and hydroxychloroquine ("triple therapy") is economical, effective, and not inferior to the combination of methotrexate plus etanercept for those who have not responded to methotrexate monotherapy. The choice of a second-line biologic agent for patients who have not responded to TNF inhibitors is often based on patient and provider preference and insurance coverage since comparative effectiveness data are sparse. Biologic DMARDs should not be combined.

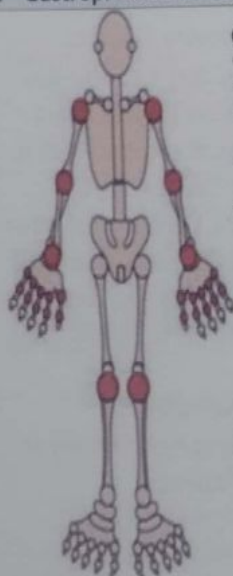
• **Combining DMARDs:** e.g., methotrexate with sulfasalazine and hydroxychloroquine

• **Combining biologics with methotrexate:** e.g., TNF inhibitor plus methotrexate

TREATMENT OF RHEUMATOID ARTHRITIS



1. Tab. Methotrexate (MTX) 2.5mg (Cytotrexate, Unitrexate) at dose 7.5mg (3 tablets) x orally once weekly OR Tab. Methotrexate 10mg (Cytotrexate) x orally once weekly gradually titrated as per patient response 15 mg orally weekly. The maximal oral dose is usually 20-25mg orally weekly.
2. Tab. Folic acid 5mg (Folic acid) orally once daily (0 - 0 - 1)
3. Low-dose corticosteroids: Tab. Prednisolone 5mg (Deltacortril) at dose 5-10mg orally once daily CMDT-2024 #Davidson's medicine (24th edition-2023): on first diagnosis, prednisolone can be started in a dose of 30 mg daily gradually reducing in 5mg increments every 2 weeks until therapy is withdrawn after about 12 weeks.
4. Non-steroidal anti-inflammatory drugs (NSAIDs):
 - ✎ Tab. Diclofenac sodium 50mg (Voren, Voltral) x at dose 50mg orally every 8-12 hourly (TDS/BD)
 - ✎ OR Tab. Naproxen sodium 250mg or 500mg (Flexin, Neoprox) x at dose 250-500mg orally twice daily
 - ✎ OR Tab. Meloxicam 7.5mg OR 15mg (Xobix, Melfix) at dose 7.5 to 15mg orally once daily
5. Gastroprotective: Cap. Pantoprazole 40mg (Zopent) x orally once daily کھانے سے 30 منٹ پہلے



Calculation

- Count swollen joints
- Count tender joints
- Measure erythrocyte sedimentation rate*
- Note patient global health assessment (1-100)
- Enter data into calculator: www.4s-dawn.com/das28

Interpretation

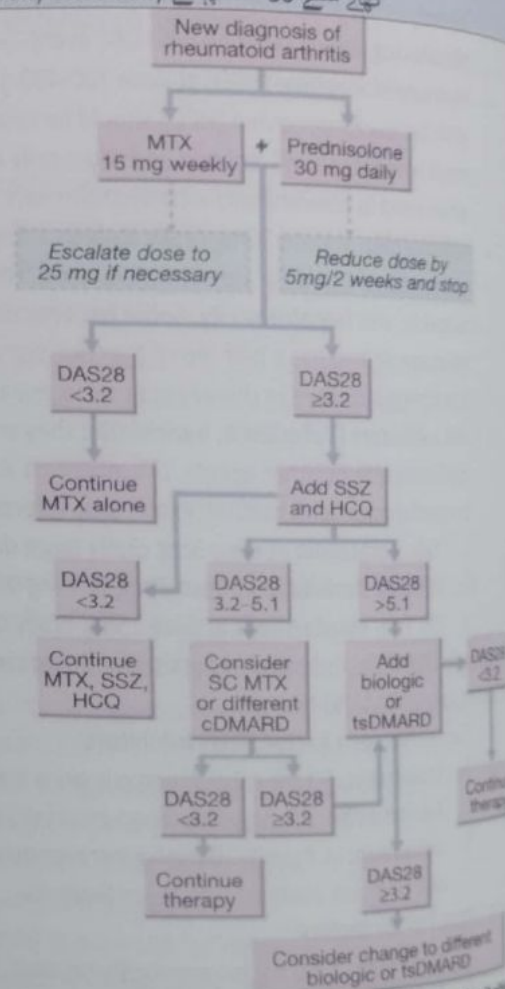
- > 5.1 High activity
- ≥3.2-5.1 Moderate activity
- 2.6-3.2 Low disease activity
- < 2.6 Remission

Calculation of the Disease Activity Score 28 (DAS28)

*Erythrocyte sedimentation rate or C-reactive protein can be used for the calculation.

Ref: Davidson's medicine (24th edition-2023)

Maintain low disease activity (months-years)



Algorithm for the management of rheumatoid arthritis

Prevention and monitoring of medication side-effects

Obtain investigation and perform vaccinations before the initiation of therapy based on the patient's individual risk and potential adverse effects of the prospective agent.

1. Baseline tests: CBC, LFTs, and serum creatinine, HCV and HBV
2. Perform TB screening in patients who will receive biologic DMARDs or tofacitinib.
3. Vaccinations for patients receiving biologic DMARDs
 - » Influenza, pneumococcus, and hepatitis B
 - » Herpes zoster

GOUTY ARTHRITIS & HYPERURICEMIA

Definition

- Gout is an inflammatory crystal arthropathy caused by the precipitation and deposition of uric acid crystals in synovial fluid and tissues. Decreased renal excretion and/or increased production of uric acid leads to hyperuricemia, which is commonly asymptomatic but also predisposes to gout.
- Acute gout flares typically manifest with a severely painful big toe (podagra) and occur most often in men following triggers such as alcohol consumption.

Etiology

Primary hyperuricemia → Idiopathic

- Increased production of purine
- Specific enzyme defects (e.g., Lesch-Nyhan syndrome, glycogen storage diseases)
- Decreased renal clearance of uric acid (idiopathic)
- No history of comorbidities or medications that affect uric acid formation or excretion

Secondary hyperuricemia

- | | |
|--|--|
| <ul style="list-style-type: none"> Decreased uric acid excretion: most common cause <ul style="list-style-type: none"> Medications: pyrazinamide, aspirin, loop diuretics, thiazides diuretics, niacin Chronic renal insufficiency, lead nephropathy Ketoacidosis; (due to, e.g., starvation, diabetes mellitus) and lactic acidosis Postmenopause Combined decreased excretion and overproduction: high alcohol consumption <ul style="list-style-type: none"> Organic acids from alcohol metabolism compete with uric acid to be excreted by the kidneys. Many alcoholic beverages contain a high level of purines | <ul style="list-style-type: none"> Increased uric acid production <ul style="list-style-type: none"> High cell turnover: Tumor lysis syndrome, Hemolytic anemias, myeloproliferative disorders, Psoriasis, Cytotoxic drugs, radiation, Down syndrome. Enzyme defects: Lesch-Nyhan syndrome, Phosphoribosyl pyrophosphate synthetase overactivity and von Gierke disease Diet rich in protein and especially purine (e.g., red meat, seafood) Obesity and Sleep apnea Hypercholesterolemia, hypertriglyceridemia Hypertension |
|--|--|

Clinical features

Asymptomatic stage

- Hyperuricemia with no symptoms
- May last ≥10 years

Acute gouty arthritis

Triggers

- Sudden ↑ in uric acid level (due to consuming a large amount of purine-rich foods or alcohol)
- Trauma, surgery
- Diuresis
- Dehydration

Most common features

- Acute severe pain with overlying erythema, decreased range of motion, swelling, warmth on affected joint (red-hot, painful & tender big-toe)
- Possibly fever, chills
- Symptoms are more likely to occur at night, typically waking the patient.
- Symptoms peak after 12–24 hours and regress over days to weeks.
- Desquamation of the skin overlying the joint may be seen during the recovery from an acute gout flare.

Recurrent gouty arthritis (Intercritical stage): The time between acute attacks - 1-2 attacks per year

- Asymptomatic
- May last up to several years

Chronic gouty arthritis

- Uncommon in these times
- Progressive joint destruction
- Formation of Tophi
 - Multiple painless hard nodules with possible joint deformities
 - May appear yellow or white because of overlying attenuated skin
 - Ulceration and discharge (chalky white substance) may occur
 - Bone tophi: urate crystal deposition in bones (elbows, knees, extensor surfaces of forearms)
 - Soft tissue tophi: urate crystal deposition in the pinna of the external ear, subcutis, tendon sheaths (e.g., at the Achilles tendon), or synovial bursae (e.g., olecranon bursa)
- Renal manifestations with uric acid nephrolithiasis and uric acid nephropathy



Location

- » Usually, monoarthritis during first attacks
 - In <20% of cases, patients present with polyarthritis during first attacks
 - Asymmetrical distribution is common if more than one joint is affected
- » Peripheral small joints in the lower extremities are especially affected.
- » **Podagra:** Metatarsophalangeal joint (MTP joint) inflammation of the big toe (the most common site)
- » **Gonagra:** Inflammation of the knee
- » **Chiragra:** Inflammation of finger joints, especially metacarpophalangeal joint of the thumb
- » **Others:** Ankle, tarsus, other toe joints, wrist, elbow

Diagnostic workup

Serum uric acid level:

- » **Reference range:** Male: 4.0-8.5 mg/dL or 0.24-0.51 mmol/L, Female: 2.7-7.3 mg/dL or 0.16-0.43 mmol/L
- » **Acute gout flare:** often elevated (hyperuricemia); may also be normal or low
- » **Intercritical stage or chronic gout**
 - Baseline levels are useful to determine the need for urate-lowering therapy.
 - A normal or low level has a very low negative likelihood ratio for (but does not rule out) a diagnosis of gout.

CBC: WBCs elevated (Neutrophilia) in acute gout attack

Serum ESR elevated in acute gout attack

Arthrocentesis and synovial fluid analysis

Gold standard investigation for diagnosing gout but should only be performed if polarized light microscopy is available and providers are trained in the procedure and interpretation.

Indications

- » Uncertain clinical diagnosis
- » Higher probability of septic arthritis

Characteristic findings

- » **Polarized light microscopy** reveals **needle-shaped and yellow monosodium urate crystals (MUC)** that are **negatively birefringent**
 - Crystals appear yellow when their optical axis is oriented parallel to the polarizer.
 - Crystals appear blue when their axis is perpendicular to the polarizer.
- » **Synovial fluid cell count:** $WBC > 2000/\mu L$ with $> 50\%$ neutrophils
- » **Gram stain:** negative; useful for ruling out septic arthritis

Ultrasound

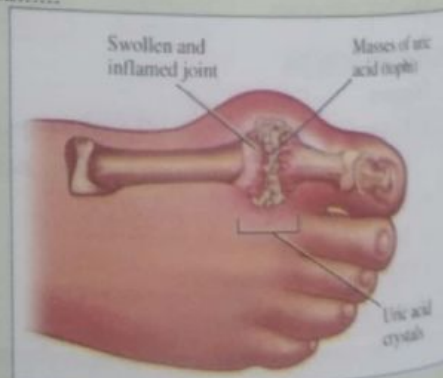
- » Signs of acute joint inflammation
- » Bone erosions
- » **Signs of urate crystal deposition**
 - Double contour sign
 - Tophi (pathognomonic for chronic gout)

X-ray

- » **Acute gout:** x-ray typically normal in acute gout; useful for ruling out a fracture in patients with posttraumatic joint inflammation
- » **Chronic gout**
 - **Punched-out lytic bone lesions with spiky periosteal appositions (overhanging edges), known as "rat bite erosions"**
 - Radiopaque in surrounding soft tissue
 - Joint space is preserved until late stages.

» **Dual-energy CT scan:** can detect crystals within deeper anatomical structures (e.g., the spine) and extra-articular sites

» **Ultrasound and dual-energy CT** can be used to confirm the diagnosis of gout



TREATMENT OF ACUTE GOUT FLARE

Asymptomatic Hyperuricemia: self-limiting <6 weeks, as a general rule, uric acid-lowering drugs should not be instituted until acute gout, renal calculi, or tophi become apparent.

Ref: AAFP guidelines, CMDT-23

Treatment of acute gout flare

1. General measure: Rest and ice the affected joint.

2. Tab. Naproxen sodium 250MG OR 500mg (Flexin, Neoprox) x 250-500mg orally, twice daily (BD)

OR Tab. Lornoxicam 8mg (Atcam, Xikarapid) x orally once daily (OD)

OR Tab. Diclofenac sodium 50mg OR 100mg (Voltral, Voren) x 50-100mg orally, twice daily (BD)

OR Cap. Indomethacin 25mg to 50mg (Indobid) x four times daily (QID)

NSAIDs: should be continued for 24 hours after complete resolution of the acute attack, then tapered quickly over 2-3 days (5 days).

OR Tab. Colchicine 0.5mg

Ref: Oxford textbook of medicine 6th edition

» Effective in acute gout within the first 12 hours (<36 hours) of symptom onset to maximize efficacy.

» Dosage: a loading dose of Tab. Colchicine 1mg (2 tablets) immediately, followed by 0.5mg every 2-3 hour until symptoms abate (or 24 hour); thereafter 0.5mg twice daily is used until resolution.

» Reduce dose and monitor closely when prescribed in patients with liver injury or mild-moderate CKD

OR Corticosteroids (Steroids & NSAIDs are equally effective in the treatment of acute gout)

» Orally Tab. Prednisolone 5mg (Deltacortril)

▪ Fixed-dose regimen: Treat for 5-10 days or until symptom resolution.

▪ A tapered regimen may reduce the risk of a rebound flare.

4 Tablets x TDS for 3 days	4 + 4 + 4 for 3 days
3 Tablets x TDS for 3 days	3 + 3 + 3 for 3 days
2 Tablets x BD for 3 days	2 + 2 + 2 for 3 days
1 Tablets x BD for 3 days	1 + 0 + 1 for 3 days
1 Tablet x OD for 3 days	0 + 0 + 1 for 3 days

▪ Note: Corticosteroids can be given at the suggested dose for 5-10 days and then simply discontinued or given at the suggested initial dose for 2-5 days and then tapered over 7-10 days.

» Intravenous or intramuscular: Inj. Methylprednisolone (Depo-medrol 40mg/ml)

▪ Dose: 40mg/day, if NPO or unable orally

» Intra-articular administration: Consider if there are 1-2 joints that are accessible

▪ Inj. Triamcinolone 40mg/ml (K-cort, Kenacort-A, Lonacort, Tricort)

▪ Dose: 10-40 mg depending on the size of the joint x intra-articular



TREATMENT OF CHRONIC GOUT

1. General management: Avoidance of hyperuricemic drugs, increase fluid & eat a healthy diet. Avoid foods that may trigger a gout flare, avoid purines food (Red meat, liver meat, and sea-food e.g., trout fish, cod fish, haddock, bacon, sardines, herring, anchovies) and limit alcohol intake (particularly beer and hard liquor).

2. Tab. Allopurinol 100mg or 300mg (Zyloric) – first line

» Dosage: The initial dose once daily of allopurinol 100mg/day per orally (50mg/day for those with stage 4 or worse CKD); the dose of allopurinol should be titrated upward every 2-5 weeks to achieve the target serum uric acid level. A typical dose of allopurinol is 300mg, but most patients require >300mg daily (maximum dose: 900mg/day) to achieve the target uric acid level.

OR Tab. Febuxistate 40mg or 80mg (Uloric, Zurig, Febuxin) – alternative first line

» Dosage: The initial dose of febuxostat is 40mg/day orally. If the target serum uric acid is not reached in weeks, the dose of febuxostat can be increased to 80mg/day & then to the maximum dose of 120mg/day.

» Febuxostat (Uloric) and allopurinol (Zyloric) are equally effective in preventing recurrent gout.

OR Second line is uricosuric agent: Tab. Probenecid (0.5 g/day orally) or Tab. Lesinurad (200 mg/day orally)



SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

Etiology of SLE

The exact etiology is unknown, but several predisposing factors have been identified, thought to be an interaction among immune dysfunction, genetic factors, and environmental factors

Genetic predisposition

- » HLA-DR2 and HLA-DR3 are commonly present in individuals with SLE.

- » Genetic deficiency of classical pathway complements proteins (C1q, C2, C4) in approx. 10% of cases.

Hormonal factors: Hyperestrogenic states (e.g., due to oral contraceptive use, postmenopausal hormonal therapy, Endometriosis) are associated with an increased risk of SLE.

Environmental factors

- » Cigarette smoking and silica exposure increase the risk of developing SLE.

- » UV light and EBV infection may trigger disease flares

- » **Medications:** Procainamide, Hydralazine, Isoniazid, Sulphonamides, Methyldopa, Phenytoin etc.

Pathophysiology of SLE

The exact pathomechanism of SLE is not fully understood, but the following two processes are the most widely accepted hypotheses:

Autoantibody development: deficiency of classical complement proteins (C1q, C4, C2) → failure of macrophages to phagocytose immune complexes and apoptotic cell material (i.e., plasma and nuclear antigens) → dysregulated, intolerant lymphocytes targeting normally hidden intracellular antigens → autoantibody production [e.g., antinuclear antibody (ANA), anti-double-stranded DNA (dsDNA) antibody]

Autoimmune reactions

- » **Type-III hypersensitivity (most common in SLE)** → antibody-antigen complex formation in microvasculature → complement activation & inflammation → damage to skin, kidneys, joints, small vessels
- » **Type-II hypersensitivity** → IgG & IgM antibodies directed against antigens on cells (RBCs) → cytopenia

Clinical features of SLE

SLE is a systemic disease characterized by phases of remission and relapse.

Some individuals only experience mild symptoms, while others experience severe symptoms and rapid disease progression. SLE can affect multiple organ systems.

Common features

- » **Constitutional:** fatigue, fever, weight loss
- » **Joints:** involve > 90% of cases
 - Arthritis and arthralgia
 - Distal symmetrical polyarthritis
- » **Skin:** involve in 85% of cases
 - **Malar rash (butterfly rash):** flat or raised fixed erythema over both malar eminences (nasolabial folds tend to be spared)
 - Raynaud phenomenon
 - **Photosensitivity** → maculopapular rash
 - **Discoid rash**
 - Oral ulcers (usually painless)
 - Non-scarring alopecia (except with discoid rashes)
 - Periungual telangiectasia

Less common features

1. **Hematological:** petechiae; , pallor, or recurrent infections due to cytopenias
2. **Musculoskeletal:** myalgia
3. **Serositis:** pleuritis and pericarditis → effusions (pleural)
4. **Kidneys:** nephritis with proteinuria (Lupus nephritis)
5. **Heart:** Pericarditis, myocarditis, endocarditis (Libman-Sacks endocarditis), Aortic valve lesions, CAD
6. **Lungs:** Pneumonitis, Interstitial lung disease, Pulmonary hypertension
7. **Vascular:** Vasculitis, Thromboembolism, Antiphospholipid syndrome
8. **CNS:** Seizures, Psychosis, Personality changes, Lupus cerebritis, Aseptic meningitis, Polyneuropathy
9. **Eyes:** keratoconjunctivitis sicca



Criteria for the classification of SLE

American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus.

A patient is classified as having SLE if any 4 or more of 11 criteria are met.

1. Malar rash
2. Discoid rash
3. Photosensitivity
4. Oral ulcers
5. Arthritis
6. Serositis
7. Kidney disease
 - a. > 0.5 g/day proteinuria, or
 - b. $\geq 3+$ dipstick proteinuria, or
 - c. Cellular casts
8. Neurologic disease
 - a. Seizures, or
 - b. Psychosis (without other cause)

9. Hematologic disorders

- a. Hemolytic anemia, or
- b. Leukopenia ($< 4000/\text{mCL}$ [$4.0 \times 10^9/\text{L}$]), or lymphopenia
- c. ($< 1500/\text{mCL}$ [$1.5 \times 10^9/\text{L}$]), or
- d. Thrombocytopenia ($< 100,000/\text{mCL}$ [$100 \times 10^9/\text{L}$])

10. Immunologic abnormalities

- a. Antibody to native DNA, or
- b. Antibody to Sm, or
- c. Antibodies to antiphospholipid antibodies based on
 - (1) IgG or IgM anti-cardiolipin antibodies
 - (2) Lupus anticoagulant, or
 - (3) False-positive serologic test for syphilis

11. Positive antinuclear antibody (ANA)

2019 EULAR/ACR classification criteria for SLE

- Criteria indication: Use in patients who have an ANA titer of $\geq 1:80$; (i.e., entry criterion; for the classification criteria).
- Further considerations: Consider other, more likely diagnoses before attributing a criterion to SLE. Criteria do not need to occur simultaneously. The occurrence of any criterion at least once is sufficient.
- SLE classification requires all of the following to be met: Entry criterion, At least one clinical criterion, Total additive score ≥ 10 points (calculated by adding the highest-weighted criteria within each domain together)

Domain	Criteria	weight
Clinical		
Constitutional	» Fever $> 38.3^\circ\text{C}$ (100.9°F)	2
Hematologic	» WBC count $< 4000/\text{mm}^3$	3
	» Platelet count $< 100,000/\text{mm}^3$	4
	» Autoimmune hemolysis	4
Neuropsychiatric	» Delirium	2
	» Psychosis	3
	» Primary generalized or focal seizures	5
Mucocutaneous	» Nonscarring alopecia	2
	» Oral ulcers	2
	» Subacute cutaneous lupus erythematosus (SCLE) Or Discoid lupus erythematosus (DLE)	4
	» Acute cutaneous lupus erythematosus ACLE	6
Serositis	» Pleural or pericardial effusion	5
	» Acute pericarditis with ≥ 2 of the following: ▪ Pleuritic chest pain ▪ Pericardial rub ▪ ECG changes (e.g., diffuse ST elevations or PR depression) ▪ Evidence of pericardial effusion on imaging studies	6
Musculoskeletal	» Joint involvement (one of the following): ▪ Synovitis of ≥ 2 joints ▪ Tenderness in ≥ 2 joints with ≥ 30 minutes of morning stiffness	4
Renal	» Proteinuria > 0.5 g in 24 hours	
	» Class II or V lupus nephritis confirmed on renal biopsy	8
	» Class III or IV lupus nephritis confirmed on renal biopsy	10
Immunological		
Antiphospholipid antibodies	» Any of the following are positive: Anticardiolipin antibodies or Anti- $\beta 2\text{GPI}$ antibodies or Lupus anticoagulant	2
Complement proteins	» $\downarrow$ C3 Complement proteins or $\downarrow$ C4 Complement proteins	3
	» $\downarrow$ C3 Complement proteins and $\downarrow$ C4 Complement proteins	4
SLE-specific antibodies	» Any of the following: Positive anti-dsDNA antibodies or Positive anti-Sm antibodies	6

Diagnostic workup for SLE

The following studies are commonly part of a minimum diagnostic workup if SLE is clinically suspected.

- ☛ **Antinuclear antibodies (ANAs)**
 - » Positive titers of $\geq 1:80$ have ~ 98% sensitivity for SLE (entry criterion for the 2019 EULAR/ACR classification criteria for SLE).
 - » If negative, consider differential diagnoses and/or follow-up with the patient regularly.
- ☛ **Antigen-specific ANAs:** Request only if ANAs are positive.
 - » **Anti-dsDNA antibodies** → Autoantibodies against double-stranded DNA (Positive in 60–70% of patients, highly specific for SLE)
 - » **Anti-Smith antibodies** → Autoantibodies against Smith antigens (non-histone nuclear proteins), Positive in < 30% of patients, but highly specific for SLE.
- ☛ **Antiphospholipid antibodies:** Screen all patients for antiphospholipid syndrome
- ☛ **Other autoantibodies commonly seen in SLE:** include antibodies to SS-A/Ro, SS-B/La, ribonucleoprotein (RNP), and Antibodies to SS-A/Ro are associated with subacute cutaneous lupus
- ☛ **Laboratory markers of disease activity and/or organ damage in SLE**
 - » **Complement levels:** ↓ C3 and/or ↓ C4 in patients with active disease
 - » **Serum ESR:** may be elevated in patients with active disease
 - » **Serum CRP:** often normal (may be elevated in patients with serositis, arthritis, or infections)
 - » **Complete blood count (CBC):** may show leukopenia, thrombocytopenia, and/or autoimmune hemolytic anemia or anemia of chronic disease
 - » **Comprehensive metabolic panel (CMP):** ↑ BUN and/or creatinine, and/or electrolyte abnormalities
 - » **Urinalysis and urine microscopy:** may show proteinuria, hematuria, and/or urinary casts
- ☛ **Radiology:** Imaging studies can help in the assessment of organ or joint involvement.
 - » **X-ray joints:** Perform in patients with articular symptoms.
 - » **X-ray or CT chest:** Perform in patients with symptoms of pulmonary involvement (e.g., ILD, pleuritis).
 - » **Echo (ETT):** Consider in patients with suspected pericardial effusion or Libman-Sacks endocarditis
- ☛ **Atherosclerotic cardiovascular disease (ASCVD) risk assessment**
 - » Recommended in all patients with SLE (ASCVD risk-enhancing factor).
 - » Includes diabetes mellitus screening, screening for lipid disorders, and a risk calculation using the 2013 ACC/AHA pooled cohort equation
 - » Patients with SLE have double the cardiovascular risk compared to patients without SLE. Cardiovascular disease is among the most common causes of death in patients with SLE.
- ☛ **Screening test:** HBsAg (HBV), Anti-HCV antibody (HCV) and PPD tuberculin test (Tuberculosis)
- ☛ **Histopathology**
 - » **Skin biopsy:** Consider in patients with atypical dermatologic presentation or no response to initial Rx.
 - » **Lupus band test (LBT):** a direct immunofluorescence staining technique used to detect immunoglobulin and complement component deposits along the dermo-epidermal junction in affected and unaffected skin in patients with SLE
 - » **Renal biopsy:** consider in case of suspected lupus nephritis, unless contraindicated

Frequency (%) of laboratory abnormalities in SLE

☛ Anemia	60%
☛ Leukopenia	45%
☛ Thrombocytopenia	30%
☛ Antiphospholipid antibodies	
» Anti-cardiolipin antibody	25%
» Lupus anticoagulant	7%
» Anti-beta-2-glycoprotein-1	25%
☛ Direct Coombs-positive	30%
☛ Proteinuria	30%
☛ Hematuria	30%
☛ Hypo-complementemia	30%
☛ Anti-nuclear antibodies	60%
☛ Anti-double-stranded DNA	95–100%
☛ Anti-Smith antibodies	20%



TREATMENT OF SLE



General principles of treatment

Advice multi-specialist consultation: Rheumatology & other departments based on the patient's clinical presentation.

Patients with SLE usually require life-long immunosuppressants.

- Management is guided by disease severity and the systems or organs affected.
- pts. should be frequently monitored for drug-induced adverse effects → CBC, LFTs, Urea, creatinine & electrolytes.
- Non-steroidal anti-inflammatory drugs (NSAIDs) can provide symptomatic relief

General measures include:

- Lifestyle changes (e.g., smoking cessation, aerobic exercise)
- Patients should be cautioned against sun exposure and should apply broad-spectrum UVA/UVB sunscreen while outdoors → SPF 30+ sunblock
- Optimize primary and secondary prevention of ASCVD and offer preconception counseling
- Admit patients with SLE and unexplained fever, severe disease (e.g., lupus nephritis, alveolar hemorrhage, NPSLE), or complications (e.g., sepsis, thrombosis), as these features are associated with increased mortality.

Disease severity: Disease severity can be classified based on the presence of clinical features and laboratory markers of disease activity and/or organ damage in SLE.

- Mild disease (no vital organs affected):** e.g., constitutional symptoms, mild arthritis rash and/or cytopenias.
- Moderate disease (no vital organs affected):** e.g., cutaneous vasculitis, serositis, RA-like arthritis, moderate rash and/or cytopenias, or no response to standard therapy
- Severe or organ-threatening disease:** e.g. nephritis, myelitis, pneumonitis, mesenteric vasculitis, severe cytopenias

Pharmacotherapy: Depending on the systems or organs affected (e.g., skin, kidneys), a specialist may decide on a different pharmacological approach.

- The cornerstone of therapy (regardless of disease activity) in all patients: Tab. Hydroxychloroquine 200mg (HCQ)
- Milder skin lesions often respond with topical corticosteroids: Betamethasone or clobetasol or Mometasone
- Minor joint symptoms can usually treat with NSAIDs: Tab. Naproxen 500mg (Flexin) x BD + Omeprazole 40mg x OD
- Mild to moderate disease (no vital organs affected): Consider the addition of oral corticosteroids with or without other immunosuppressive agents to achieve remission.
- Severe or organ-threatening disease

Induction therapy

- High-dose IV glucocorticoids and other immunosuppressive agents
- Used until symptom remission or low disease activity is achieved

Maintenance of remission

- Oral Hydroxychloroquine; with or without lower dose oral corticosteroids (Prednisolone at dose 5-10mg)
- AND/OR immunosuppressants agents (cyclophosphamide, Mycophenolate mofetil, Azathioprine, methotrexate, or tacrolimus) or biological agents (Belimumab or Rituximab)
- Disease flares: Adjust therapy based on the severity of organ involvement.

Overview of the recommended treatment for patients with non-renal SLE

	Mild to moderate disease	Severe disease
1. Standard therapy (for all patients):	Tab. Hydroxychloroquine 200mg (HCQ, Plaquin-H, Planquinil) at dose 200 (or 400) mg/day orally and should not exceed 5mg/kg/day. Drug monitoring for retinal toxicity is recommended annually.	
2. Additional therapy		
Corticosteroids	» Tab. Prednisolone (Deltacortril) at dose 30-40mg (≤0.5mg/kg/day) is initially for short term, then maintenance dose at ≤7.5mg x PO x once daily	» Inj. Methylprednisolone (Solu-Medrol) at dose 250-1000mg IV over 30 minutes daily for 3 days » Then initiate Tab. Prednisolone at dose 0.5 mg to 0.7 mg per kg once daily x PO, gradually taper to a maintenance dose at ≤7.5mg x PO x once daily
Immunosuppressant	» Tab. Methotrexate 10-25mg once a week in 1-3 divided doses with Tab. Folic acid 5mg x OD » Or Tab. Azathioprine 1.5 mg to 2.5 mg/kg/day x PO x BD » If there is no response to Hydroxychloroquine 200mg x OD Plus Prednisolone at dose ≤7.5mg	» Tab. Azathioprine 1.5 mg to 2.5 mg/kg/day x PO x BD Or Tab. Mycophenolate mofetil 1 to 1.5g x PO x BD Or Cyclophosphamide 500mg (7-25mg/kg) x IV every 2 weeks for 6 doses, consider mesna administration » Biological agents: Indicated if persistently active disease, frequent flares despite adequate treatment » Belimumab 10mg/kg x IV weekly 0, 2, 4 then monthly or Rituximab 375mg/M2 every week for 4 weeks or 1g every 2 weeks for 2 weeks

LUPUS NEPHRITIS

- ☞ Most dangerous specific manifestation because of its high morbidity and mortality
- ☞ Can manifest as nephritic syndrome and/or nephrotic syndrome
- ☞ **Common:** found in up to 50% of individuals with SLE at presentation
- ☞ **Pathophysiology:** Mesangial and/or subendothelial deposition of immune complexes (e.g., anti-dsDNA antibodies, anti-Sm antibodies) → expansion and thickening of mesangium, capillary walls, and/or glomerular basement membrane

ABBREVIATED HISTOPATHOLOGIC CLASSIFICATION OF LUPUS NEPHRITIS

☞ Class-I	» Minimal mesangial disease
☞ Class-II	» Mesangial proliferative disease
☞ Class-III	» Focal glomerular disease
☞ Class-IV	» Diffuse glomerular disease; can be further subdivided into: ▪ Segmental glomerular disease (Class IV-S) ▪ Global glomerular disease (Class IV-G)
☞ Class-V	» Membranous glomerular disease
☞ Class-VI	» Advanced sclerosing disease

△ Lupus nephritis

C/C:

- » Clinical features of SLE
- » Hypertension
- » Edema
- » Hematuria

Investigation

- » Diagnostic investigation of SLE
- » Elevated creatinine
- » **Urinalysis:** proteinuria, hematuria, cellular casts (RBCs, hemoglobin, granular, tubular, or mixed)
- » **Spot urine protein:** creatinine ratio: proteinuria ≥ 0.5 g/g

Kidney biopsy

- » Indicated in patients with either:
 - Unexplained $\uparrow$ creatinine
 - Proteinuria ≥ 1.0 g/g
 - Proteinuria ≥ 0.5 g/g and hematuria or cellular urinary casts
- » **Findings:** immune complex-mediated glomerulonephritis

Rx Treatment of Lupus nephritis

General principles of management

- ☞ Provide patient education, counseling and support.
- ☞ Consult a nephrologist, rheumatologist and consider other sub-specialty
- ☞ Induction and maintenance therapy is generally indicated in patients with class III or IV lupus nephritis.
- ☞ All patients should receive standard therapy for lupus and individualized management of chronic kidney disease (CKD).

Pharmacological management

☞ Induction therapy

- » Inj. Methylprednisolone (Solu-Medrol) at dose 250–1000mg IV over 30 minutes daily for 3 days
- » **PLUS**, other immunosuppressants
- » **Tab. Mycophenolate mofetil** 1000 mg or 1500 mg orally twice daily
- » Or Inj. Cyclophosphamide 500mg x IV every 2 weeks for six doses (**Euro-lupus regimen**) or 3–6 monthly IV pulses (0.5–1 g/m²) for induction (**NIH regimen**).

☞ Maintenance of remission

- » **Tab. Prednisolone** 5mg (Deltacortril)
- » **PLUS**, other immunosuppressants
- » **Tab. Mycophenolate mofetil** 1 to 1.5g x PO x BD
- » Or **Tab. Azathioprine** 1.5 mg to 2.5 mg/kg/day x PO x BD

☞ Adjunctive therapy: ACEI inhibitors and Hydroxychloroquine

- ☞ **Combination of Belimumab** can improve renal response when added to cyclophosphamide or mycophenolate mofetil.

☞ Refractory or relapsing disease: Rituximab may be considered.

- » Rituximab is usually reserved for life-threatening or organ-threatening manifestations that have failed conventional therapies.
- » **Dosage:** Rituximab 375mg/M² every week for 4 weeks or 1g every 2 weeks for 2 weeks.

PLANTAR FASCIITIS



Sharp heel pain

- » Pain is worse with first step in the morning or after a period of rest, then improves with walking
- » Pain may be worse again at the end of the day with prolonged standing/weight-bearing may also improve with stretching, massage, & rest
- » May prefer to walk on toes initially
- » Relieved by ambulation
- » Common to have symptoms bilaterally tender to palpation at medial tuberosity of calcaneus

On physical examination:

- » The patient usually has a point of maximal tenderness at the anteromedial region of the calcaneus. The patient may also have pain along the proximal plantar fascia.
- » The pain may be exacerbated by passive dorsiflexion of the toes or by having the patient stand on the tips of the toes.

Investigation:

- » X-Ray: Initially not necessary, often normal, may show plantar heel spur
- » CT/MRI: may be useful for surgical planning



- » Stretching of the foot and calf
- » Orthotics or night splinting
- » Rest and raise your foot on a stool when you can
- » put an ice pack (or bag of frozen peas) in a towel on the painful area for up to 20 minutes every 2 to 3 hours
- » Wear shoes with cushioned heels and good arch support
- » Use insoles or heel pads in your shoes
- » Try regular gentle stretching exercises
- » Try exercises that do not put pressure on your feet
- » Try to lose weight if you're overweight

1. **Tab. Paracetamol + Tramadol** (Distalgescic, Tonoflex-P)
OR **Tab. Diclofenac sodium 50mg** (Voltral, Voren)
OR **Tab. Naproxen sodium 500mg** (Neoprox, Flexin)
1-0-1 x orally twice daily (BD)
OR **Tab. Meloxicam 15mg** (Mobix, Melfix)
OR **Tab. Lornoxicam 8mg** (Xikarapid, Atcam)
0-0-1 x orally once daily (OD)

2. **Cap. Esomeprazole 40mg** (Eskem, Nexum, Esso)
OR **Cap. Omeprazole 40mg** (Ruling, Omega, Risek)
1-0-0 (OD)

کھاتے سے 30 منٹ پہلے

POLYMYALGIA RHEUMATICA

Polymyalgia rheumatica

C/C:

Clinical Presentation

- » Proximal limb-girdle pain and morning stiffness in the appropriate host
- » Constitutional manifestations include fever, malaise and weight loss.

Diagnosis: Examination reveals muscle tenderness but no true muscle weakness

Investigation

- » Elevated ESR >50 mm/hr.
- » Elevated CRP
- » Normochromic anemia
- » Elevated platelets
- » Leucocytosis



(Oxford textbook of rheumatology)

1. **Tab. Prednisolone 5mg** (Deltacortril, Rapicort)
 - » **Oral dosage:** Initial low dose at 15mg/day, should be gradually tapered after disease control or fixed dose 5mg for 3 months.
 - Usually rapid symptomatic relief 2-4 weeks
 - **If symptoms improve:** slowly taper and eventually stop corticosteroids
 - **No improvement after 2 weeks or relapse:** increase dose
2. **Tab. Paracetamol + Tramadol** (Distalgescic, Tramol plus)
OR **Tab. Naproxen sodium 500mg** (Neoprox, Flexin)
1-0-1 x orally twice daily (BD)
OR **Tab. Meloxicam 15mg** (Mobix, Melfix)
OR **Tab. Lornoxicam 8mg** (Xikarapid, Atcam)
0-0-1 x orally once daily (OD)
3. **Cap. Omeprazole 40mg** (Ruling, Omega, Risek)
OR **Cap. Esomeprazole 40mg** (Eskem, Nexum, Esso)
0-0-1 (OD)

کھاتے سے 30 منٹ پہلے

GIANT CELL ARTERITIS (GCA/TEMPORAL ARTERITIS)

- Definition: Giant cell arteritis (GCA) is a type of autoimmune vasculitis in elderly women > 50 years of age, also known as **Temporal Arteritis**, that causes chronic inflammation of large and medium-sized arteries, in particular the carotid arteries, its major branches, aorta and **Temporal artery** is the most commonly affected
- Sex: women > male
- Peak incidence: 70 – 79 years (rarely seen in patients < 50 years)
- Etiology:
 - Unknown; presumed to be autoimmune, possible contributing factors include:
 - Genetic predisposition: Human leukocyte antigen = HLA-DR4
 - Viral infections: Parvovirus B19
 - Association with polymyalgia rheumatica (PMR): up to 50% of patients with GCA also have PMR
- Pathogenesis: T-cells & monocytes are recruited to the vessel wall → result in an inflammatory response

DIAGNOSIS

CLINICAL FEATURES	INVESTIGATION
Constitutional symptoms » Fever, weight loss, night sweats » Symptoms of anemia: fatigue and malaise » Myalgia, arthralgia (mainly of the shoulder and hip joints) Clinical features of arterial inflammation » New-onset unilateral (or bilateral) temporal headache » Jaw claudication: jaw pain when chewing due to maxillary artery involvement » Vision loss: due to involvement to ophthalmic artery and its branches ▪ Scintillating scotoma ▪ Amaurosis fugax or permanent blindness » Diplopia » Symptoms of PMR (polymyalgia rheumatica) » Morning stiffness Physical exam » Scalp tenderness » Hardened and tender temporal artery » Palpation of the temporal area may reveal → absent pulse and knot-like swelling » Findings of PMR: distal extremity swelling	» Inflammatory markers: initial laboratory test in suspected Giant cell arteritis (GCA) » Elevated ESR, specifically ≥ 50 mm/hour → due to Rouleaux formation of RBCs. » Elevated CRP » Additional blood tests » CBC: normal or mild thrombocytosis, leukocytosis, or normochromic anemia » Liver studies: normal or $\uparrow$ ALP, $\uparrow$ ALT and AST, or $\downarrow$ albumin » Coagulation profile: normal or $\uparrow$ fibrinogen » Gold standard: Temporal artery biopsy Indications » Consider in all patients with suspected GCA » High clinical suspicion for GCA despite inconclusive findings on imaging » Finding: Focal granulomatous inflammation with formation of giant cells Important considerations: The minimum length of biopsy is 1.5-2 cm (avoid short biopsies). Histopathology may be falsely negative due to skip lesions. Short biopsies may miss the inflammation and consequently miss the diagnosis; therefore, longer biopsies are needed.

First line radiology:

Duplex ultrasound or CTA of the temporal arteries (with/without the axillary arteries)

Findings:

- » Edema and thickening of the vessel wall (halo sign)
- » Noncompressible artery (compression sign)
- » Stenosis and occlusion

TREATMENT OF GIANT CELL ARTERITIS (TEMPORAL ARTERITIS)

Initial high-dose corticosteroids therapy (induction therapy) for approximately 2–4 weeks is indicated for all patients with newly diagnosed GCA or recurrent GCA symptoms.

» **Tab. Prednisolone 5mg (Deltacortril)**

Dosage: at dose 1mg/kg/day (or maximum 60–80 mg/day) should be initiated immediately for 1 month then tapered, and a temporal artery biopsy performed promptly thereafter.

» **For patients with visual loss (Ischemic organ damage):** Consider initial pulse therapy with IV steroids

IV Inj. Methylprednisolone 1g (Solu-Medrol) at dose 1000mg IV over 30 minutes daily for 3 days

Oral Tab. Prednisolone 5mg (initially, or following pulse therapy)

» **Maintenance therapy**

» Initiate after acute symptoms have resolved.

» Slowly taper glucocorticoids to the lowest dose needed to control symptoms.

» **Length of treatment:** no consensus; generally, ≥ 2 years

» Administer prophylactic measures to prevent complications of glucocorticoid therapy as needed.

» **Adjunct therapy**

» **Glucocorticoid-sparing therapy**

Indications: Consider in patients who relapse or are at high risk of complications from long-term glucocorticoid therapy, May be used to decrease the dose of glucocorticoids

Options

▪ **Tocilizumab** (inhibitor of the IL-6 receptor, is FDA-approved for GCA → Can reduce the prolonged use of prednisone and decrease the risk of disease flare.

▪ Methotrexate

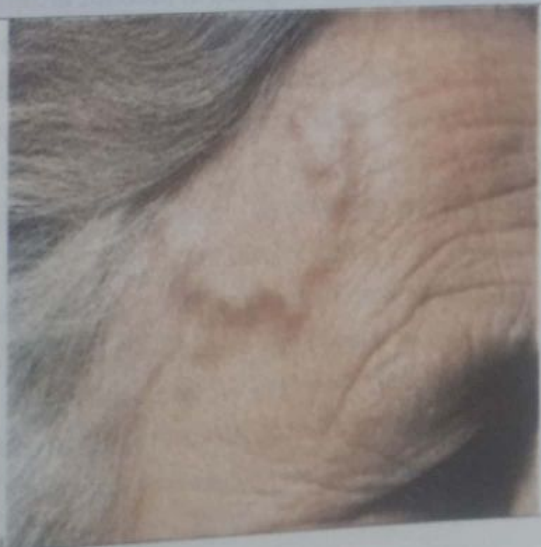
» **Low-dose aspirin:**

▪ Not routinely recommended

▪ Consider in patients with preexisting cardiovascular or cerebrovascular disease

Inflamed
temporal
artery

Giant cell arteritis



PSORIATIC ARTHRITIS (PsA)

Definition: Psoriatic arthritis or PsA is a type of inflammatory arthritis that primarily affects the hands, feet, and/or spine and associated in about 30% of patients with psoriasis.

Clinical features

Arthritis: Multiple patterns arthritis may be present.

The patterns or subsets of joint involvement in psoriatic arthritis include the following:

1. **Symmetric polyarthritis:** similar appearance to rheumatoid arthritis, usually, fewer joints are involved than in rheumatoid arthritis.
2. **Oligoarthritis:** Typically asymmetric; ≤ 4 joints affected, that may lead to considerable destruction of the affected joints.
3. **Distal interphalangeal (DIP) joint first affected,** asymmetrically distributed in $> 50\%$ of individuals.
4. **Arthritis mutilans (severe deforming arthritis with osteolysis):** Destruction of interphalangeal joints through bone resorption, resulting in the collapse of the soft tissue of the affected area (telescoping fingers or "opera glass hand")
5. **Spondylitic form (Axial involvement):** Sacroiliitis and spinal involvement predominate often occurs in conjunction with other subtypes, 50% of these patients are HLA-B27 positive.

Accompanying features

- » **Enthesitis (enthesopathy):** Affected joint & tendons, e.g., of the calcaneal tendon or the plantar fascia
- » **Dactylitis:** inflammation and swelling of the fingers and/or toes ("sausage digits") of one or more digits.
- » **Tenosynovitis:** Inflammation of a tendon and its respective synovial sheath.
- » **Nail involvement:** Nail pitting and onycholysis frequently accompany DIP involvement.
- » **Uveitis:** An inflammation of the middle layer of the eye (uvea)

Diagnostic workup

General principles for diagnosis of psoriatic arthritis

- » Diagnosis is mainly on clinical basis, based on patient and family history and clinical features.
- » Laboratory investigations are usually obtained as a part of the inflammatory arthritis workup.
- » Imaging – can support the diagnosis and help estimate severity (Sensitivity = MRI $>$ Ultrasonography $>$ X-ray)
- » Consult rheumatology for all patients.
- » **Laboratory test:** May be obtained to rule out other diagnoses but are not typically required to make a diagnosis of psoriatic arthritis.
 - » **Inflammatory markers:** ESR $\uparrow$ (in 50% cases) and CRP may be $\uparrow$
 - » **Uric acid level:** may be high, reflecting the active turnover of skin affected by psoriasis.
 - » **HLA-B27:** present in = 25% of patients
 - » **Rheumatoid factor, ANA and anti-CCP antibodies:** Negative in = 95% of patients
- » **Imaging:** Radiological findings are most helpful in distinguishing the disease from other forms of arthritis.
 - » X-ray of the affected area (e.g., hands, spine) – X-ray may appear normal in early disease, especially in patients with axial involvement.
 - » **Fingers:** Appearance of a sharpened pencil (pencil-in-cup deformity of DIP joints) – Marginal erosions of bone and irregular destruction of joint and bone, which, in the phalanx
 - » **Spine:** syndesmophytes, asymmetric paravertebral ossification, unilateral sacroiliitis
 - » **Doppler ultrasound:** may show early erosions, synovitis, and enthesophytes
 - » **MRI:** may show focal erosions, synovitis, and/or bone marrow edema

THE CASPAR CLASSIFICATION CRITERIA FOR PSORIATIC ARTHRITIS

These classification criteria are not diagnostic but can provide guidance in clinical practice.

Interpretation: Inflammatory articular disease (joint, spine or enthesitis) with a total score points ≥3 from the following (1 point each unless stated):

	Criteria	Score
Clinical features	» Current psoriasis	2
	» Family history of psoriasis first- or second-degree relative	1
	» Psoriatic nail dystrophy	1
	» Current dactylitis	1
	» History of dactylitis	1
Investigation findings	» Negative IgM rheumatoid factor	1
	» Radiologic signs of PsA (Juxta-articular new bone)	1



TREATMENT OF PSORIATIC ARTHRITIS (PsA)

General principles of the treatment

- » Treatment depends on disease severity and the presence of certain features and/or comorbidities.
- » A treat-to-target approach with a target of remission or low disease activity is recommended.
- » Consult a rheumatologist before starting pharmacotherapy.

General treatment

- » Patient education to understand the breadth, episodic nature and variability of disease is important.
- » **Encourage lifestyle modifications.**
 - » Smoking cessation
 - » Low-impact physical activity
 - » Weight loss may play a therapeutic role to limit clinical impact.
- » Recommend physical therapy and occupational therapy

Medication

- » **Disease-modifying anti-rheumatic drugs (DMARDs):** Mainstay of treatment for most patients with PsA. In patients with active psoriatic arthritis (PsA), a TNF inhibitor biologic agent is recommended as first-line agent. If a TNF inhibitor is contraindicated or not tolerated, methotrexate (or non-biologic agents, such as leflunomide, sulfasalazine, cyclosporine, or apremilast) may be effective.
- » **Conventional DMARDs:** Methotrexate (DOC, also effective for skin disease), sulfasalazine, Leflunomide
- » **Targeted synthetic DMARDs:** Apremilast, Tofacitinib
- » **Biologic DMARDs, e.g.:**
 - » **TNF- α inhibitors (first line):** Etanercept, Adalimumab, Infliximab
 - » **IL-17 inhibitors:** Secukinumab, Ixekizumab
 - » **IL-12/23 inhibitors:** Ustekinumab, Guselkumab
 - » **Abatacept:** Effective when cDMARD therapy fails, but is less efficacious than biologic treatments
- » **NSAIDs:** Naproxen sodium 500mg (Flexin) x BD or Tab. Lornoxicam 8mg (Atcam) x BD
 - » May be trialed as initial treatment in patients with very mild disease (limited evidence of efficacy)
 - » Preferred over DMARDs in certain patients, e.g., those with axial disease or predominant enthesitis
 - » Can also be prescribed for symptomatic relief
- » **Gastroprotective:** Cap. Omeprazole 40mg (Omezol) OR Cap. Esomeprazole 40mg (Esso) x Once daily
- » **Intraarticular glucocorticoids:** used for symptomatic relief, can control isolated synovitis or enthesitis

REACTIVE ARTHRITIS (REITER SYNDROME)

- Introduction:** Reactive arthritis (formerly known as Reiter syndrome) is a postinfectious autoimmune condition that is most commonly preceded by bacterial infection of the gastrointestinal or urinary tract. It is categorized as a seronegative spondyloarthropathy and is associated with HLA-B27. Reactive arthritis often affects young adults and manifests with musculoskeletal and/or extra-articular symptoms.
- The classic diagnostic triad of Reactive Arthritis:** 1. Arthritis (Can't Walk), 2. Conjunctivitis (Can't see), and 3. Urethritis (can't pee). It is only seen in about 1/3 of patients. Reactive arthritis is primarily a clinical diagnosis.

Etiology

- Postinfectious autoimmune disorder:**
- » After STIs (Post-urethritis) with Chlamydia (common) or *Ureaplasma urealyticum*
 - » After gastrointestinal infection with *Shigella*, *Yersinia*, *Salmonella*, or *Campylobacter*
 - » The spectrum of pathogens known to cause reactive arthritis after infection include: *Bartonella henselae*, *Mycobacterium*, *Borrelia*, *Staphylococcus*, SARS-CoV-2 and mycobacteria, including *M. leprae*, which causes leprosy (Hansen's disease)

Diagnostic workup

- Laboratory test**
- » **Blood tests:** Consider in all patients although findings are often nonspecific.
 - ↳ CBC: WBC ↑, platelets ↑
 - ↳ Inflammatory markers: ESR ↑, CRP ↑
 - ↳ Rheumatoid factor, ANA and anti-CCP antibodies: negative
 - » **Arthrocentesis with synovial fluid analysis:** indicated if the diagnosis is unclear or may be required to exclude crystal arthritis and articular infection (septic arthritis)
 - ↳ WBC count: ↑ (5000-50,000/mm³; neutrophil predominant)
 - ↳ Gram stain and cultures: typically, negative
 - ↳ Crystals: absent
 - » **Stool culture:** Perform only in ongoing diarrhea; send culture for *Shigella*, *Yersinia*, *Salmonella*, and *Campylobacter*.
 - » **STI (Sexually transmitted infections) testing:** indicated for patients with risk factors for STIs
 - ↳ Perform RT-PCR on urine or high vaginal swab culture for genitourinary chlamydia.
 - ↳ Consider diagnostic studies for gonorrhea if there is concern for disseminated gonococcal infection.
 - ↳ Consider HIV testing: if the presentation is atypical (e.g., widespread dermatologic manifestations) or if the patient has risk factors for bloodborne viruses
- Radiological test**
- » **X-ray of affected region:** in suspected case of arthritis – may show erosions & bone proliferation
 - » **Suspected synovitis or enthesitis**
 - » **MRI with IV gadolinium or ultrasound:** in Suspected synovitis or enthesitis – may include synovial hypertrophy, hypervascularization of soft tissue, tendon thickening
 - » **In case of suspected cardiac manifestations/cardiac involvement**
 - ↳ ECG to screen for atrioventricular blocks and pericarditis
 - ↳ Echocardiogram for aortic regurgitation
 - » **Suspected ocular manifestations:** slit lamp examination for keratitis and anterior uveitis

General principles of management

- Acute reactive arthritis**
- » Management is primarily supportive as reactive arthritis is typically self-limiting
 - » Acute reactive arthritis should be treated with rest, NSAIDs and analgesics.
 - » **Identify and treat underlying infections:** Genitourinary chlamydia.
 - » Refer patients to rheumatology and physiotherapy; consider additional referrals (e.g., ophthalmology, cardiology) as needed.
- Chronic reactive arthritis (persistence of symptoms > 6 months) or severe disease:**
- » DMARDs e.g., sulfasalazine may be required.

Clinical features

- » Latency period: 1–4 weeks
- » Musculoskeletal symptoms
 - » Oligoarthritis (sometimes polyarthritis) – Acute onset, often asymmetrical with a migratory character. Occurs predominantly in the lower extremities
 - » Enthesitis and osteitis: causes low back pain and stiffness.
 - » Sacroiliitis (15–20% of patient)
 - » Dactylitis
- » Extra-articular symptoms
 - » Conjunctivitis, iritis, episcleritis, or keratitis, Uveitis (rarely)
 - » Dermatologic manifestations
 - Balanitis circinata (skin lesions of the glans resembling psoriasis)
 - Keratoderma blenorrhagicum (hyperkeratinization of the palms and soles)
 - Pustular psoriasis
 - Nail dystrophy with subungual hyperkeratosis
 - » Urethritis
 - » Oral ulcers
 - » Cardiac manifestations
 - Aortic regurgitation
 - Atrioventricular blocks
 - Pleural-Pericarditis
 - » CNS manifestations:
 - Peripheral neuropathy
 - Seizures
 - Meningoencephalitis
 - » Symptoms from preceding infection
 - Diarrhea
 - Urogenital tract symptoms (dysuria, pelvic pain, prostatitis)



TREATMENT OF REACTIVE ARTHRITIS

Treatment of Arthritis

- » NSAIDs: first-line treatment for all symptomatic patients
 - ↳ Choose medication based on patient characteristics; start with a high dose and titrate to the lowest effective dose.
 - ↳ No NSAID has shown greater efficacy over another in trials; long-acting agents e.g., naproxen may improve adherence.
- » Glucocorticoids: indicated in patients with inadequate response or contraindications to NSAIDs
 - ↳ Monoarthritis or oligoarthritis: intraarticular glucocorticoids
 - ↳ Polyarthritis or severe extra-articular disease: systemic glucocorticoids, e.g., prednisone
- » DMARDs: indicated in patients with chronic (> 6 months) or severe disease
 - ↳ Options include either conventional DMARDs (e.g., sulfasalazine or methotrexate) or biopharmaceuticals.
 - ↳ There is limited research about the effect of DMARDs on patients with reactive arthritis; sulfasalazine currently has the largest evidence base.
- » Antibiotics
 - ↳ Long courses of antibiotics (up to 6 months) are used by some specialists to manage reactive arthritis.
 - ↳ Evidence to support this approach is mixed.

» **Treatment of Extraarticular manifestations:** Treatment should be overseen by the relevant specialist or consider referral

» Ocular

- ↳ Management of anterior uveitis, keratitis, and episcleritis follows standard best practice for these conditions.
- ↳ Treatment usually involves symptomatic relief and topical or systemic glucocorticoids.

» **Dermatologic:** Treatment typically involves topical steroids and keratolytics.

» Cardiac

- ↳ Pericarditis: high dose glucocorticoids or DMARDs
- ↳ Depending on severity, AV block may require a pacemaker and aortic regurgitation valve replacement.

» Management of underlying infections

↳ Treat active infections.

- Treat all patients with genitourinary chlamydia (even if asymptomatic).
- Consider treatment for patients with severe bacterial gastroenteritis, especially if immunocompromised.

↳ For sexually transmitted infections:

- Perform contact tracing for sexual partners and offer testing.
- Gonorrhea/chlamydia infection: Treat all sexual partners from the last 60 days. OR treat the most recent partner if no partners in the last 60 days.

↳ Counsel on safe sex practices.

SEPTIC ARTHRITIS

- ☞ **Definition:** Septic arthritis is an infection of the joint space, which can occur in a native joint or a prosthetic joint. Septic arthritis is the most rapid and destructive joint disease.
- ☞ **Routes of infection include**
 - » **Hematogenous spread (most common)**
 - From a distant site: Abscesses, wound infection, septicemia
 - Disseminated infection: Gonorrhea
 - » **Direct inoculation:** iatrogenic, penetrating trauma
 - » **Contiguous spread:** septic bursitis, osteomyelitis
- ☞ **Risk factors:** Prosthetic implant, Intra-articular injections, pre-existing joint disease (Rheumatoid arthritis), Diabetes mellitus, compromised immunity, Age > 80 years, Psoriasis, Advance CKD, IV drug use, Endocarditis
- ☞ **Etiology:** Staphylococcus aureus (Most common), Streptococci (2nd MCC), N. gonorrhoeae (seen in healthy and sexually active), Pseudomonas aeruginosa (healthcare-associated infections), Staphylococcus epidermidis (prosthetic joint infections), Mycobacterium tuberculosis, Borrelia burgdorferi (Lyme disease)

Clinical features

- ☞ The onset is acute, with pain, swelling, and heat of the affected joint worsening over hours.
- ☞ Classical triad of fever, joint pain, and restricted to movement
- ☞ **Arthritis usually monoarticular**
 - » **Most commonly affected joints:** knees (followed by hip, wrists, shoulders, and ankles)
 - » Joints are swollen, red, warm, and painful.
- ☞ Patients with pre-existing condition arthritis may present with multiple joint involvement.
- ☞ Risk factors for multiple joint involvement include rheumatoid arthritis, associated endocarditis, and infection with group B streptococci.

Diagnostic workup

Any red, painful joint with a reduced range of motion should be considered infectious until proven otherwise. The absence of fever does not rule out a diagnosis of septic arthritis.

- ☞ **Arthrocentesis (Aspirate joint) with synovial fluid analysis and culture (Gold standard test)**
 - » **Appearance:** often yellow-green and turbid (nonspecific)
 - » **Cell count**
 - **WBC count:** ↑ (WBC count of the synovial fluid is always inflammatory (> 2000/mcL [$2 \times 10^9/L$]), usually exceeds 50,000/mcL ($50 \times 10^9/L$), and often is > 100,000/mcL ($100 \times 10^9/L$).
 - Neutrophil (polymorphonuclear cells) dominance of > 90%
 - » **Glucose levels:** lower than blood glucose levels
 - » **Gram stain:** Positive in 75% of staphylococcal infections and in 50% of gram-negative infections.
 - To guide empiric antibiotic therapy for native joint infection
 - A negative Gram stain does not rule out septic arthritis.
 - » **Synovial fluid culture & sensitivity:** Positive in 70-90% of cases & to guide targeted antibiotic therapy
- ☞ **Laboratory finding**
 - » **Blood cultures and sensitivity:**
 - Patients with fever or acute onset of symptoms
 - Positive in 25-50% of cases of septic arthritis and 25-70% of cases of gonococcal arthritis
 - » **CBC:** Leukocytosis
 - » **Inflammatory markers:** CRP and ESR may be elevated (nonspecific).
 - » **BUN/Urea, Creatinine, Electrolytes & LFTS:** to guide antibiotic selection
 - » **Uric acid:** may be normal
 - » **Additional test**

- **Serum procalcitonin level:** Consider if diagnostic arthrocentesis is not feasible or in patients with comorbid inflammatory arthritis. Levels > 0.2 – 0.3 ng/mL provide supportive evidence of a bacterial infection of bones or joints.
- **Coagulation profile:** Perform prior to arthrocentesis in patients on anticoagulation.
- **Culture and PCR testing for *N. gonorrhoeae*:** For suspected gonococcal arthritis
- **X-rays of the affected joint:** Usually normal early in the disease; however, evidence of demineralization may develop within days of onset.
- **MRI and CT scan:** More sensitive in detecting fluid in joints that are not accessible to physical examination (e.g., the hip). Bony erosions and narrowing of the joint space followed by osteomyelitis and periostitis may be seen within 2 weeks.

TREATMENT OF SEPTIC ARTHRITIS

The effective treatment of septic arthritis requires appropriate antibiotic therapy together with drainage of the infected joint. Hospitalization is always necessary. If the likely causative organism cannot be determined clinically or from the synovial fluid Gram stain, treatment should be started with broad-spectrum antibiotic coverage effective against staphylococci, streptococci, and gram-negative organisms.

- **Admit patient to hospital**
- **Perform urgent investigations**
- **Empiric antibiotic therapy:** Septic arthritis of a native joint (after diagnostic arthrocentesis has been performed), Antibiotic therapy should be adjusted when culture results become available; the duration of antibiotic therapy is usually 4–6 weeks (If Gonococcal arthritis typically 7 days). Initiate pathogen-specific antibiotics once the antibiogram is available (preferably in consultation with infectious diseases specialists)
 - **Inj. Vancomycin 1g** (Vinjec, Vancotic) x twice daily (or 15–20mg/kg 8–12 hourly adjusted for age, weight, and renal function)
 - **PLUS, one of the following**
 - **Inj. Ceftriaxone 1g OR 2g** (Oxidil, Rocephin, Titan) x Once daily (or every 12 hours if concomitant meningitis or endocarditis is suspected)
 - OR **Inj. Cefotaxime 1g** (Claforan, Wintax) x Thrice daily (8 hourly)
- **Pain management:** Oral and/or IV analgesics or NSAID (caution in older patients), Consider local ice-packs
 - **Oral NSAIDs:**
 - **Tab. Naproxen sodium 500mg** (Flexin, Neoprox) x Twice daily
 - OR **Tab. Diclofenac sodium 50mg OR 75mg** (Voren, Arnil) x Twice daily
 - OR **Tab. Lornoxicam 8mg** (Atcam, Xikarapid, Acabel) x Orally once daily
 - **OR IV analgesics:** **Inj. Ketorolac 30mg/ml** (Toradol, Ketor), dilute in 4ml x BD/TDS
- **Gastroprotective in patient with risk of GI bleed due to NSAIDs**
 - **Oral PPIs:** **Cap. Omeprazole 40mg** (Omezol, Ruling) OR **Cap. Esomeprazole 40mg** (Esso, Nexum) x OD
 - OR **IV PPIs:** **Inj. Omeprazole 40mg** (Omezol, Ruling) OR **Inj. Esomeprazole 40mg** (Esso, Nexum) x OD
- **VTE prophylaxis as needed:** **Inj. Enoxaparin sodium 60mg/0.6ml or 80mg/0.8ml** (Clexane) x at dose 100 IU/kg (1.5mg/kg) x subcutaneous (SC) x Once daily
 - **Clexane 60mg/0.6ml** (= 6000anti-Xa IU/0.6ml) or **Clexane 80mg/0.8ml** (= 8000anti-Xa IU/0.8ml)
- **Aspirate joint (arthrocentesis)**
 - Perform serial needle aspiration to dryness (1 – 3 times daily or as required)
 - Consider arthroscopic drainage if needle aspiration difficult
 - Consider synovial biopsy at arthroscopy for tissue for PCR analysis for tuberculosis
- **Arrange physiotherapy:** Early regular passive movement, progressing to active movements once pain controlled and effusion not re-accumulating
- **Early orthopedic consultation for surgical intervention** (Debridement, exchange arthroplasty, or arthrodesis).
- **Effective drainage is usually achieved through early arthroscopic lavage and debridement.**
- **Options for treating prosthetic joint infections depend, in part, on the timing of the infection and include chronic suppression, debridement without removal of the prosthesis, or one- or two-stage exchange of the prosthesis.**

FIBROMYALGIA SYNDROME

Definition: Fibromyalgia (FM) is a neurosensory disorder characterized by chronic musculoskeletal pain. The Etiopathogenesis of this condition are not fully understood, but, notably, there is no identifiable inflammation that causes the musculoskeletal symptoms. Patients typically present with functional symptoms (fatigue, unrefreshing sleep, morning stiffness) and often have a history of psychiatric disorders (depression, generalized anxiety disorder). Physical examination reveals characteristic tender points over multiple areas of the body with no signs of inflammation (no notable swelling, deformity, or erythema). Findings from laboratory tests are normal. Although this disorder is benign, it causes patients significant psychological strain and discomfort.

Epidemiology: Prevalence: 2–3%, **Sex:** Female > Male (2:1), **Peak incidence:** 20–50 years ↑ chances in ↑ age

DIAGNOSIS OF FIBROMYALGIA (FM)

Fibromyalgia (FM) is a clinical diagnosis

The 2016 American College of Rheumatology (ACR) criteria take into account:

- » Symptom duration of at least 3 months
 - » Patient self-reporting using the fibromyalgia score:
 - Widespread pain or tenderness in up to 19 different regions of the body (widespread pain index)
 - Presence and severity of symptoms such as fatigue, sleep disturbance, depression, headache, and cognitive impairment (symptom severity scale)
 - Self-reporting criteria are met if Widespread pain index (WPI) ≥ 7 and symptoms severity scale (SSS) ≥ 5 OR widespread pain index (WPI) 4–6 and SSS ≥ 9
 - » Presence of generalized pain: pain in ≥ 4 regions (upper left, upper right, axial, lower left, lower right)
- Traditionally, a tender-point examination was performed based on the 1990 ACR diagnostic criteria:
- » Symptom duration of at least 3 months
 - » Tender points: ≥ 11 of 18 FM-associated localized areas of pain
 - » Pain-affected areas: all four quadrants of the body

Laboratory values and imaging findings are normal (helpful for excluding other causes or comorbidities).

△ Clinical features of Fibromyalgia (FM)

C/C:

Common symptoms

- » Chronic, widespread pain, primarily at points where muscles and tendons attach to bone (tender points)
- » Headache, fatigue
- » Morning stiffness
- » Unrefreshing sleep
- » Cognitive dysfunction (known as fibro fog): Poor memory, difficulty concentrating, and lack of clarity of thought
- » Paresthesias
- » Autonomic dysfunction: Digestive problems, weight fluctuation, palpitations, sexual dysfunction, night sweats

Common associations: The following disorders can manifest with symptoms that sometimes resemble those seen in Fibromyalgia, and these conditions may occur alongside Fibromyalgia.

- » **Functional somatic syndromes:** e.g., chronic fatigue syndrome, irritable bowel syndrome (IBS), tension or migraine headaches, chronic pelvic and bladder syndromes
- » **Psychiatric disorders:** Depression, Generalized anxiety disorder (GAD)
- » **Sleep disorder:** e.g., sleep movement disorders such as restless leg syndrome
- » **Inflammatory rheumatic diseases:** e.g., systemic lupus erythematosus, rheumatoid arthritis

TREATMENT OF FIBROMYALGIA (FM)



Initial approach

- » **Patient education:** Explain that the condition, though painful, is benign, and recommend coping strategies such as relaxation exercises.
- » **Lifestyle modifications:** regular physical activity, dietary recommendations, sleep hygiene
- » **Pharmacotherapy initially with monotherapy (single drug):** Low-dose tricyclic antidepressants (TCA), selective serotonin-norepinephrine reuptake inhibitors (SNRIs), or anticonvulsants
- » **Avoid long term use of narcotic medications:** Opioids (Tramadol, Tapentadol)
- » **Consider comorbidities in treatment planning:** Sleep disorders, anxiety, depression

Non-responders

- » Multidisciplinary management approach (with rheumatology, psychiatry) & adequate pain management
- » **Psychological interventions:** Cognitive-behavioral therapy
- » **Physiotherapy:** Stretching, hydrotherapy, and heat application
- » Combination therapy with the drugs mentioned above

1. Cap. Duloxetine 30mg OR 60mg (Dulan, Lyta, Cymbalta, Zenbar)
0-0-1 (Once daily), may increase up to 60mg/day
OR Cap. Pregablin 50mg, 75mg OR 100mg (Gabica, Zeegap, Syngab)
1-0-1 (Twice daily)
OR Tab. Amitriptyline 25mg (Tryptanol, Amitin)
0-0-1 (Once daily), may increase up to 50mg/day
2. Tab. Paracetamol 325mg + Tramadol 37.5mg (Distalgesic, Tonoflex-P)
OR Tab. Diclofenac sodium 50mg (Voren, Voltral, Arnif)
OR Tab. Diclofenac potassium 50mg (Caflam, Dyclo-P)
1-0-1 (BD) OR 1-1-1 (TDS)
OR Tab. Meloxicam 15mg (Mobix, Melfix)
OR Tab. Lornoxicam 8mg (Xikarapid, Atcam)
0-0-1 x orally once daily (OD)
3. Gastroprotective: Cap. Esomeprazole 40mg (Eskem, Nexum, Esso)
OR Cap. Omeprazole 40mg (Ruling, Omega, Risek)
0-0-1 (OD)

کھانے سے 30 منٹ پہلے



FROZEN SHOULDER (ADHESIVE CAPSULITIS)

- ☞ **Definition:** Adhesive capsulitis is a chronic inflammation and fibrosis of the joint capsule, characterized by insidious and progressive severe restriction of both active and passive shoulder range of motion, in the absence of a known intrinsic disorder of the shoulder.
- ☞ **Epidemiology:** More common in women than in men, onset > 40 years of age (Usually 40 – 70).
- ☞ **Etiology:** associated with diabetes mellitus, thyroid disorders (esp. hypothyroidism), shoulder injuries (e.g., rotator cuff tear, proximal humerus fracture), and prolonged immobilization
- ☞ **Classifications of adhesive capsulitis**
 - » **Primary (idiopathic):** No underlying cause or precipitating event.
 - » **Secondary:** Attributable to an underlying cause (e.g., diabetes mellitus, thyroid dysfunction) or precipitating event (trauma, prior surgery to affected shoulder).

Clinical features

- ☞ Typically affects the nondominant shoulder
- ☞ Dull shoulder pain
- ☞ Shoulder stiffness
- ☞ **Decreased shoulder active & passive range of motion of the glenohumeral joint in all planes, especially:**
 - » External rotation
 - » Passive abduction (restricted to < 90°)

Diagnostic Approach

- ☞ **Clinical examination**
 - » **Positive coracoid pain test:** Pain elicited by direct pressure on the coracoid
 - » **Positive shoulder shrug test:** Inability to abduct the arm to 90° in the plane of the body and to hold that position briefly is considered positive.
- ☞ **Diagnostic workup**
 - » **Plain X-rays** (anteroposterior, lateral, & axillary views of the glenohumeral joint). X-ray is typically normal in frozen shoulder
 - » **Ultrasound:** Thickening of the coracohumeral ligament & the soft-tissue structures in the rotator cuff interval
 - » **MRI/MR arthrogram:** Decreased capsular volume and changes in rotator interval dimensions may be present; may show evidence of a thickened capsule.
 - » **Other test, if indicated:** TSH, FBS, HBA1C



- ☞ **Physical therapy:** early mobilization and exercise
- ☞ **Non-steroidal anti-inflammatory drugs (NSAIDs):**
 - » **Tab. Diclofenac sodium 50mg** (Voren, Voltral) x at dose 50mg orally every 8-12 hourly (TDS/BD)
 - » **OR Tab. Naproxen sodium 250mg or 500mg** (Flexin, Neoprox) x at dose 250-500mg orally twice daily
 - » **OR Tab. Meloxicam 7.5mg OR 15mg** (Xobix, Melfix) at dose 7.5 to 15mg orally once daily
 - » **OR Tab. Lornoxicam 4mg OR 8mg** (Acabel) at dose 4-8mg orally once daily
- ☞ **Gastroprotective:** **Cap. Esomeprazole 40mg** (Eskem, Esso) **OR Cap. Omeprazole 40mg** (Ruling, Omega, Risek) 0 – 0 – 1 (OD)
- ☞ **Oral corticosteroid** (burst and taper) for severe pain
- ☞ **Intraarticular corticosteroid injection:** Inj. Triamcinolone
- ☞ **Surgical treatment** if symptoms persist after 9 months of conservative management
- ☞ **Prognosis:** self-limiting (improvement typically takes > 1 year)
- ☞ **Complications:** atrophy of the deltoid and spinatus muscles



MIGRAINE HEADACHE (آدھے سر کا درد 'درد شقیہ')

△ **Migraine Headache** (آدھے سر کا درد 'درد شقیہ')

- C/C:**
- **Pain:** Crescendo pattern, Headache usually pulsating/throbbing, but not always, unilateral. Pain is aggravated with routine physical activity.
 - **Duration:** 4 to 72 hours
 - Patient retreats to dark, quiet room
 - Nausea, vomiting and anorexia
 - **Photophobia:** Sensitivity to light
 - **Phonophobia:** Sensitivity to sound
 - **Osmophobia:** Fear to smell/odors
 - **Migraine with aura (Focal disturbances of neurological function)** → Visual disturbances occur commonly and may consist of field defects (Scotoma); of luminous visual hallucinations such as stars, sparks, unformed light flashes (photopsia), geometric patterns, or zigzags of light; or of some combination of field defects and luminous hallucinations (scintillating scotomas). Other focal disturbances such as aphasia or numbness, paresthesias, clumsiness, dysarthria, dysequilibrium, or weakness in a circumscribed distribution may also occur.

Potential triggers: Emotional or physical stress, Lack or excess of sleep, bright light, loud noises, Variations in caffeine intake, alcoholic beverages, chocolate, cheese, nitrates, tyramines, Hormonal changes, menstruation or use of OCPs

DIAGNOSTIC CRITERIA WITHOUT AURA

At least five attacks fulfilling the following criteria: Untreated headache lasting 4 to 72 hours

Group A (2 of 4):

1. Unilateral headache
2. Throbbing or pulsating pain
3. Moderate to severe pain that inhibits ability to function

4. Pain aggravated by routine physical activity

Group B (1 of 2):

1. Presence of nausea or vomiting
 2. Presence of photophobia and Phonophobia
- Underlying disorders that may cause secondary headaches must be ruled out



ACUTE MIGRAINE HEADACHE TREATMENT

- **Inj. Ketorolac 30mg/1ml** (Toradol, Ketor) at dose 30-60mg + **Inj. Metoclopramide 10mg/2ml** (Maxolon, Metaclo) x diluted in 3ml 0.9% NS x IV once.
- ↳ OR **Inj. Ketorolac 30 to 60mg** (Toradol, Ketor) x IM once
- ↳ OR **Inj. Diclofenac sodium 75mg/3ml** (Voren) x IM once

Migraine-specific medications: Do not combine below agents

• **Triptans:**

- ↳ **Zavegepant 10mg** (ZAVZPRET nasal spray) at dose 10mg as a single spray in one nostril. **Max 10mg/24hour**
- ↳ OR **Zolmitriptan 2.5mg nasal spray** (Zolmipine, Zolmist) at dose 5mg 2 intranasal sprays once; may repeat once after 1 hour as needed.
- ↳ OR **Tab. Zolmitriptan 2.5mg** (Zomig, Triptan, Limigzole) x at dose 1.25 to 2.5 mg PO once; may repeat once after 2 hours as needed (max. dose 10 mg/24 hours)
- ↳ OR **Tab. Sumatriptan 85mg + Naproxen sodium 500mg** (Synflex-M, Sumoxen, Imtaxen) x One tablet once at the onset of the headache. Maximum 2 tablets/24 hours.
- ↳ OR **Tab. Sumatriptan 50mg or 100mg** (Imigran, sumig, Sumatec) at dose 50mg to 100mg x Once, may repeat once after 2 hours if needed. (Maximum: 200mg/day).
- **Ergotamine:** **Tab. Ergotamine 1mg + Caffeine 100mg** (Migril, Cafergot) at dose 1-2 tab at the onset of headache.



TREATMENT OF MILD TO MODERATE MIGRAINE

- **Behavioral modification:** Avoid "triggers, Regular sleeping patterns and Minimize stress
- **Tab. Paracetamol 500mg** (Panadol, Calpol) 2 tablets x TDS
Dosage: 500mg to 1000mg x TDS
- OR **Tab. Diclofenac sodium 50mg or 75mg** (Voren, Arnif)
Dosage: 100mg – 150mg mg two divided doses per day
- OR **Tab. Naproxen sodium 250mg or 500mg** (Flexin, Proxen)
Dosage: 250mg to 500mg x two times a day

Note: Long term NSAIDs (Mefenamic acid, Naproxen) causes peptic ulcer, PPIs such as Cap. Omeprazole 40mg (Risek) or Esomeprazole 40mg (Nexum) should be added once daily.



Recommendations for use of prophylactic migraine medication

- Start with low dose and titrate slowly
- Decrease in headache frequency may be imperceptible the 1st month:
 - » For first month, 10% decrease in frequency is considered successful
 - » Improvement is cumulative, may take 6 months to reach efficacy
 - » Success = 50% reduction in headache frequency
- After a 6-month period of headache stability, periodically evaluate.

OTHER EFFECTIVE MEDICATION FOR MIGRAINE PROPHYLAXIS:

- Tab. Candesartan 8mg (Advant) at dosage 8mg upto 32mg once daily
- Tab. Verapamil (Calan, Isoptin, Zavera)
- Tab. Divalproex sodium 500mg (Epival CR)
- Tab. Amitriptyline 10mg: Probably effective; unrelated to antidepressant activity.
- Dosage:** 25mg orally at bedtime; increase dose by 25mg every 2 to 4 weeks twice weekly, until response is adequate.
- Tab. Venlafaxine: at dose 37.5 mg – 150 mg (extended release), orally once daily.
- Tab. Riboflavin (Vitamin B2): 400mg daily
- Tab. Pizotifen 10mg (Mosigar) x OD/BD OR Syp. Pizotifen 5mg/5ml (Mosigar) x 10ml HS/BD
- ❖ NSAIDs: use to prophylaxis known triggers (e.g., start before menses for menstrual migraine)
- ❖ Topiramate may cause weight loss, Consider side-effect of weight loss for obese patients.
- ❖ Avoid frequent use of opioids due to the risk of rebound headaches and medication overuse headache.

Prophylaxis of the chronic migraine with Monoclonal Antibodies Against Calcitonin Gene-Related Peptide

Generic Name	Brand Name	Dose, Rout & Duration	Possible Side-effects
Eptinezumab	Inj. Vyepti 100mg/1ml	100mg Intravenously (IV) every 3 months	Hypersensitivity reaction during infusion, nasopharyngitis.
Erenumab	Inj. Aimovig 70mg/1ml	70–140mg subcutaneously (SC) once x monthly	Injection site reactions, constipation, muscle cramps, antibody development.
Fremanezumab	Inj. Ajovy 225mg/1.5ml	225mg subcutaneously x (SC) once monthly	Injection site reactions, antibody development
Galcanezumab	Inj. Emgality 120mg/1ml	120mg daily x 2 doses, followed by 120mg monthly	Injection site reactions, antibody development.
Atogepant	Tab. Qulipta 10mg, 30mg and 60mg	10 to 60mg x once per day	Nausea, constipation and fatigue (low energy) and decreased appetite (anorexia)

Rx

For Prophylaxis prescription #1

1. Tab. Topiramate 25mg or 50mg (Hitop, Topamax, Toratej)
Dosage: Start at dose 25mg Once at night titrated weekly by 25mg x twice daily, titrated up to 200mg/day.

OR Tab. Valproic acid 250mg or 500mg (Epival, Dapakan) at dose 500-1000mg in 2 divided doses x 1-0-1 (BD)

OR Tab. Propranolol 10mg or 40mg (Inderal, Cardinal)

Dosage: 80mg to 240mg in 2-4 divided doses x BD/TDS/QID

NSAIDs may be given as adjunctive therapy for 1-2 weeks

2. Tab. Naproxen 250mg or 500mg (Flexin, Neoprox) at dose 250mg to 500mg x Twice daily (BD)
OR Tab. Diclofenac sodium 50mg (Voren, Voltral) at dose 50mg to 100mg in 2-3 divided doses x BD/TDS

Gastroprotective: Long term NSAIDs causes gastritis

3. Cap. Omeprazole 40mg (Risek, Ruling)
0-0-1 (OD)

ایک گولی روزانہ ایک بار کھانے سے 30 منٹ پہلے

Rx

For Prophylaxis prescription #2

1. Cap. Flunarizine 5mg (Sibelium, Lunar) at dose 10mg (2 capsule) orally once daily at night
OR Tab. Divalproex sodium 500mg (Epival CR)
0-0-1 (One tablet once at nighttime)

NSAIDs may be given as adjunctive therapy for 1-2 weeks

2. Tab. Diclofenac Potassium 50mg (Cafam, Dyclo-P, Sofac-P)
OR Tab. Aceclofenac 100mg (Acenac, Acemed, Alkeris)
1-0-1 (BD)

Gastroprotective: Long term NSAIDs causes gastritis

3. Cap. Esomeprazole 40mg (Esso, Nexum)
0-0-1 (OD) ایک گولی روزانہ ایک بار کھانے سے 30 منٹ پہلے
4. ± Adjunct: Tab Propranolol 10mg (Inderal, Cardinal)
1-0-1 (10mg x BD), 2-0-2 (20mg x BD)

CLUSTER HEADACHE

Cluster Headache

Episodes of severe unilateral, non-throbbing periorbital, recurrent ("in clusters" over time) pain occur daily for several weeks and are often accompanied by one or more of the following:

- Ipsilateral nasal congestion
- Rhinorrhea
- Lacrimation
- Redness of the eye
- Others: Horner syndrome (ptosis, pupillary miosis, and facial anhidrosis or hypohidrosis).

During attacks, patients are often restless & agitated

Episodes typically occur at night, awaken the patient

Duration of pain: last between 15 minutes & 3 hrs.

Spontaneous remission then occurs, and the patient remains well for weeks or months before another bout of closely spaced attacks.

Bouts may last for 4 to 8 weeks and may occur up to several times per year.

During a bout, many patients report alcohol triggers an attack; others report that stress, glare, or ingestion of specific foods occasionally precipitates attacks

Pathogenesis: unclear but may relate to activation of cells in the ipsilateral hypothalamus, triggering the trigeminal autonomic vascular system.

NSAIDs may be add as adjunctive therapy

- Tab. Naproxen 250mg or 500mg (Flexin, Neoprox) x BD
- OR Tab. Diclofenac sodium 50mg or 100mg (Voren, Voltal) x BD
- Tab. Diclofenac Potassium 50mg (Caflam, Cyclo-P, Sofac-P) x BD
- OR Tab. Aceclofenac 100mg (Acenac, Acemed, Alkeris) x BD

Rx

TREATMENT OF ACUTE CLUSTER HEADACHE

- Inhalation of 100% Oxygen '12 to 15L via a non-rebreather mask for 15 minutes.
- OR Inj. Sumatriptan 6mg/0.5ml (Imigran) x Subcutaneously
Dosage: 4-6mg once subcutaneously, may repeat once after 2 hours if needed. (Maximum dose: 12mg/day)
- OR Zolmitriptan 2.5mg nasal spray (Zolmipine, Zolmist)
Dosage: spray 2 nostril (5mg) once at the time of headache onset, may repeat once after 2 hours if needed.
Maximum dose: 10mg per 24 hours
- OR viscous Lidocaine at dosage of 1mg 4-6% solution intranasally is sometimes effective.

Rx

For Prophylaxis prescription #1

1. Tab. Prednisolone 5mg (Deltacortril, Rapicort)
3-Tablets TDS for 3 days (3-3-3 for 3 days)
2-Tablets TDS for 3 days (2-2-2 for 3 days)
1-Tablets TDS for 3 days (1-1-1 for 3 days)
1-Tablets BD for 3 days (1-0-1 for 3 days)
1-Tablet OD for 3 days (0-1-0 for 3 days)
2. Cap. Omeprazole 40mg (Risek, Ruling)
OR Cap. Esomeprazole 40mg (Nexum, Esso)
0-0-1 (OD)
ایک گولی روزانہ ایک بار کھانے سے 30 منٹ پہلے

Rx

For Prophylaxis prescription #2

1. Tab. Verapamil 40mg or 80mg or 240mg (Calan, Isoptin)
Standard Dosage: start at 240mg daily, increase by 80mg every 2 weeks to 960mg daily, with routine ECG to monitor the PR interval.
OR Tab. Topiramate 25mg or 50mg (Hitop, Topamax, Torate)
Dosage: start initially 25mg once at night titrated weekly by 25mg x twice daily, titrated up to 200mg (max: 400mg/day)
OR Tab. Lithium carbonate 400mg (Neurolith SR, Lithotrop SR)
Dosage: start at 300mg daily, titrating according to serum levels and treatment response up to a typical total daily dose of 900-1200mg, divided three or four times daily.
OR Tab. Divalproex sodium 500mg (Epival CR)
0-0-1 (one tablet at night)

TENSION TYPE HEADACHE (TENSION HEADACHE)

- ☞ Tension-type headache (TTH) is a primary headache disorder
- ☞ The most common type of headache overall.
- ☞ = 86% of the population will have had at least one episode in their lifetime.
- ☞ More common in female > male, Peaked incidence at age is 30 to 39 years.

ETIOLOGY

- ☞ The exact pathophysiology of tension headaches remains unknown.
- ☞ **Exacerbating factors:** fatigue, lack of sleep, poor posture, anxiety, stress, depression

△ Tension headache.

C/C:

- » Headache **episodic** in nature
- » **Duration:** Headaches last 30 minutes to a couple of days.
- » **Holocranial or bifrontal, band-like headache** (mild to moderate intensity)
- » Headache is dull, pressing, non-pulsating (vice-like) quality
- » Headache does not increase with exertion
- » Maximum of one autonomic symptom (phonophobia or photophobia)
- » **No nausea, vomiting, or aura**
- » Palpation of muscles of the head may reveal increased pericranial tenderness.

HIGHYIELD PHARMACOTHERAPY

1. **Anti-migraine preparations** are not recommended unless the patient has morbid migraine headaches.
2. **Episodic tension-type headache:** Paracetamol and NSAIDs such as Naproxen, Ibuprofen, Diclofenac sodium, diclofenac potassium and Aceclofenac
3. **Chronic tension-type headache and frequent episodic type:** consider prophylactic therapy with amitriptyline, topiramate, SSRIs.
4. Avoid prolonged use (>15 days per month) of NSAIDs for chronic tension headache, as this may cause medication overuse headaches.
5. **All types of tension-type headache:**
 - » Triptans are not indicated for the treatment of isolated TTH
 - » Opioids should be avoided.

GENERAL NON-MEDICATION TREATMENT

- ☞ Consider if there is a significant decrease in patient's quality of life.
- ☞ **Lifestyle and behavioral modification:** exercise, weight reduction, reduction of caffeine intake, smoking cessation, stress reduction, sleep hygiene.
- ☞ **Psycho-behavioral treatments** (cognitive-behavioral therapy, relaxation training, physical therapy, biofeedback)

Rx

TREATMENT OF ACUTE ATTACK

- ☞ **Inj. Ketorolac 30mg/1ml** (Toradol, Ketor) x IV/IM
 - » **IV:** 30-60mg, diluted in 5-6 ml 0.9% NS x IV x Stat
 - » **IM:** 60mg (2ml) intramuscular x Once
- ☞ **OR Inj. Diclofenac sodium 75mg/3ml** (Voren, Voltal) x IM

Prescription #1

For the prophylaxis of chronic tension headache

1. **Tab. Amitriptyline 25mg** (Tryptanol, Amyline, Amitin)

Dosage: 10-25mg orally at night; increase dosage by 10-25mg every week, until response is adequate.
- ☞ **OR Tab. Topiramate 25mg or 50mg** (Hitop, Topamax, Torate)

Dosage: start at 25mg once at night titrated weekly by 25mg twice daily (BD), titrated up to 200mg (Max: 400mg/day)

NSAIDs maybe added adjunctive therapy with PPI for 7-14 days

2. **Tab. Aceclofenac 100mg** (Acenac, Acemed, Alkeris)

OR Tab. Diclofenac potassium 50mg (Cafiam, Dyclo-P, Sofac)

1-0-1 (BD)
3. **Gastroprotective: Cap. Omeprazole 40mg** (Risek, Ruling)

0-0-1 (OD)

ایک گولی روزانہ ایک بار کھانے سے 30 منٹ پہلے

Rx

Prescription #2

1. **Cap. Fluoxetine 20mg** (Flux, Depex) x 1-0-0 (OD)

OR Tab. Venlafaxine 75mg (Efexor XR, Vendep) x 0-0-1 (OD)

One tablet x OD, if there is no response, consider increasing the dose. **N.B.** SSRI takes 8-12 weeks to show clinical effect and much safer than TCAs (Amitriptyline, Nortriptyline)

NSAIDs maybe added adjunctive therapy with PPI for 7-14 days

2. **Tab. Diclofenac sodium 50mg** (Voltal, Voren)

OR Tab. Naproxen sodium 500mg (Flexin, Neoprox)

1-0-1 (BD)
3. **Gastroprotective: Cap. Esomeprazole 40mg** (Nexum, Essal)

0-0-1 (OD)

ایک گولی روزانہ ایک بار کھانے سے 30 منٹ پہلے

TRANSIENT ISCHAEMIC ATTACKS (TIA)

Definition: Transient ischemic attack (TIA) refers to temporary, focal cerebral ischemia that results in reversible neurological symptoms without acute infarction (CT scan/MRI findings show no signs of infarction).

CLINICAL FEATURES

Neurological manifestations

- Acute, transient focal neurological symptoms
- Typically, symptoms last < 1 hour (the majority of cases resolve in <15 minutes).
- Possibly **AMAUSIS FUGAX**
- Symptoms depend on the affected territory
 - Embolic: often a single, discrete episode lasting hour rather than minutes
 - Lacunar stroke/small vessel disease
 - Large vessel disease/low-flow state: often recurrent episodes lasting minutes
- Atypical symptoms may be seen.

Features suggesting a specific underlying cause

- Atrial fibrillation: palpitations, irregular heart rate
- Carotid artery stenosis: carotid bruit
- Endocarditis: fever, heart murmur, history of IV drug abuse
- Aortic dissection: chest pain, hypotension
- Paradoxical embolism: features of DVT

DIAGNOSTIC WORKUP

- Initial test: CT brain (without contrast) < MRI (more sensitive for early stroke detection)
- Routine tests (see ischemic stroke for interpretations): CBC, RBS, BUN, Creatinine, Electrolytes, LFTs, Coagulation profile.
- Additional test for evaluating etiology: Fasting lipid profile (8-12 hours fasting), HbA1c, TSH, Pregnancy test, Chest x-ray, ECG, troponin, Electrocardiography, Lumbar puncture, EEG, CT angiography (CTA) or MR angiography, CT perfusion or MRI perfusion.

ABCD² RISK ASSESSMENT SCORE FOR TIA

	CRITERIA	POINTS
Age	≥ 60 years	1
B.P	SBP ≥140 OR DBP ≥90	1
Clinical features	Speech impairment only	1
	Unilateral weakness	2
Duration of symptoms	10-59 minutes	1
	≥ 60 minutes	2
Diabetes	Present	1
Interpretation:		
Score 0-3: low two-day stroke risk (1%)		
Score 0-3: moderate two-day stroke risk (4%)		
Score 0-3: high two-day stroke risk (8%)		



TREATMENT OF TRANSIENT ISCHEMIC ATTACK

- Lifestyle changes (Mediterranean diet, aerobic exercise) & reduction of risk factors (B.P, hyperlipidemia, diabetes)
- ASCVD Prevention: Hypertension control, diabetes control, high statins therapy and long-term antiplatelet therapy
- Identify and treat any complications such as Atrial fibrillation or atrial flutter, valvular disease and large artery disease
- Provide early rehabilitation and mobilization.

1. Treatment of hypertension – see hypertension.

Tab. Lisinopril 5mg or 10mg (Zestril) x OD

Dosage: Initial oral dose 5mg upto 10mg x once daily

OR Tab. Losartan 50mg or 100mg (Eziday, Cozaar) x OD,

Dosage: Initial oral dose 50mg x once daily

OR Tab. Amlodipine + Valsartan (Newday, Avsar)

» **Dosage:** Initially one tab. Newday 5/80mg x OD

» **Strength available:** 5/80mg, 5/160mg, 10/160mg

2. Treatment of diabetes if diabetic – see DM endocrinology

3. High intensity statin therapy:

Tab. Atorvastatin 40mg (Lipitor, Lipiget) x OD

Dosage: 40mg up to 80mg x once daily (OD)

OR Tab. Rosuvastatin 20mg (X-Plended, Rovista) x OD

Dosage: 20mg up to 40mg x once daily (OD)

4. Anti-platelets therapy: All patients in whom anticoagulation is not indicated should be treated with antiplatelet therapy to reduce the frequency of TIAs and the incidence of stroke.

» Low-risk TIA (ABCD² <4):

Tab. Aspirin 75mg (Loprin, Ascard) x OD

OR Tab. Clopidogrel 75mg (Lowplat, Plavix) x OD

» High-risk TIA (ABCD² ≥ 4 or minor stroke): DAPT (Dual antiplatelet therapy) – Tab. Clopidogrel 300mg

(Lowplat, Plavix) at loading dose 300-600mg, followed by

Tab. Clopidogrel 75mg (Lowplat, Plavix) x OD, PLUS Tab.

Aspirin 75mg (Ascard, Loprin) x OD, continue for 21-90

days then switch to antiplatelet monotherapy with Tab.

Aspirin 75mg (Ascard, Loprin) x orally, OD

✓ Dual antiplatelet therapy (DAPT) with aspirin and clopidogrel for 90 days after a TIA or stroke due to 70-99% stenosis of an intracranial artery is also recommended.

✓ Tab. Cilostazol 100mg BD had similar efficacy as aspirin at long-term stroke prevention in an Asian population with less risk of hemorrhage.

5. Gastroprotective: Tab. Pantoprazole 40mg (Zopent) x once daily (OD) ایک گولی روزانہ ایک بار کھاتے سے 30 منٹ پہلے

ISCHEMIC STROKE (CEREBRAL INFARCTION/CVA)

- ☞ **Definition:** Ischemic stroke (Cerebral infarction) is an acute neurological condition caused by impaired cerebral blood flow (vascular occlusion or systemic hypoperfusion). Which results in ischemia and neuronal injury
- ☞ **Other definitions to differentiate stroke:**
 - » **Stroke:** acute neurologic injury caused by ischemia or hemorrhage
 - » **Transient ischemic attack:** temporary, focal cerebral ischemia that results in neurologic deficits without acute infarction or permanent loss of function (previously defined as lasting < 24 hours)
 - » **Hemorrhagic stroke:** cerebral infarction due to hemorrhage
 - » **Intracerebral hemorrhage:** bleeding within the brain parenchyma
 - » **Subarachnoid hemorrhage:** bleeding into the subarachnoid space
 - » **Intraventricular hemorrhage:** bleeding within the ventricles

MODIFIABLE AND NONMODIFIABLE RISK FACTORS FOR STROKE

NON-MODIFIABLE RISK FACTORS (FIXED RISK FACTOR)

- | | |
|--|---|
| <ul style="list-style-type: none"> ☞ Advance age: (> 65 years of age) ☞ Male sex (> female) ☞ Family history of CVS (MI) or cerebrovascular disease (CVA). ☞ Previous history of: <ul style="list-style-type: none"> » Transient ischemic attacks (TIA)/stroke » Myocardial infarction » Peripheral vascular disease | <ul style="list-style-type: none"> ☞ Migraine with aura ☞ Ethnicity (Asian, Black, Hispanic) ☞ Genetic disorders <ul style="list-style-type: none"> » Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) » Sickle cell disease |
|--|---|

MODIFIABLE RISK FACTORS

- | | |
|---|--|
| <ul style="list-style-type: none"> ☞ Systemic hypertension – Highest risk factor ☞ Hypercholesterolemia (High LDL cholesterol) ☞ Obesity ☞ Diabetes mellitus ☞ Coronary artery disease (CAD): Atherosclerosis ☞ Cardiovascular disease: Carotid artery stenosis, Atrial fibrillation, congestive heart failure, Infective endocarditis. ☞ Excessive alcohol use ☞ Cigarette smoking (Tobacco use) | <ul style="list-style-type: none"> ☞ Coagulopathy: Protein 'C' or 'S' deficiency ☞ Hyperhomocysteinemia ☞ Recreational drug use: IV drugs, cocaine, heroin, amphetamines, and ecstasy ☞ OCP use & Hormone replacement therapy. ☞ Chronic kidney disease, Polycythaemia ☞ Sedentary lifestyle: minimal physical activity ☞ Suboptimal diet: High salt intake, inadequate fruit and vegetable intake |
|---|--|

ETIOLOGY

1. **Embolic strokes (= 20% of all strokes)**
 - » Most commonly affect the middle cerebral artery (MCA)
 - » Dislodged emboli can affect multiple cerebral vascular territories simultaneously.
 - » **Cardiac emboli:** Atrial fibrillation, Atrial or ventricular thrombi, Rheumatic heart disease, ventricular aneurysms
 - » **Atheroemboli:** Internal carotid artery, Aortic arch
 - » **Infectious emboli:** Bacterial endocarditis
 - » **Paradoxical embolism:** venous thromboembolism (especially due to deep vein thrombosis) in patients with right-to-left cardiac shunt (e.g., persistent foramen ovale or atrial septal defect)
 - » **Spectacular shrinking deficit:** Distal migration of the embolus leads to recanalization of the affected vessel and rapid clinical improvement after symptom onset.
2. **Thrombotic strokes (= 40%)**
 - » **Large vessel atherosclerosis** (= 20%)
 - » **Small vessel occlusion:** Lacunar infarct (= 20%)
3. **Global cerebral ischemia**
 - » Systemic hypoperfusion
 - » Shock or bilateral large artery atherosclerosis of carotid arteries)
 - » Common during cardiac surgeries
 - » Can result in watershed infarct
 - » Repeated episodes of hypoglycemia
 - » Severe and/or chronic hypoxia
4. **Hypercoagulable states**
 - » Inherited thrombophilia (e.g., factor V Leiden mutation, protein C or S deficiency)
 - » Polycythemia
 - » Hormonal contraceptive use
 - » Hormone replacement therapy
 - » Sickle cell disease
5. **Vasculitis:** Temporal/Giant cell arteritis, SLE
6. **Arterial dissection:** due to trauma or fibromuscular

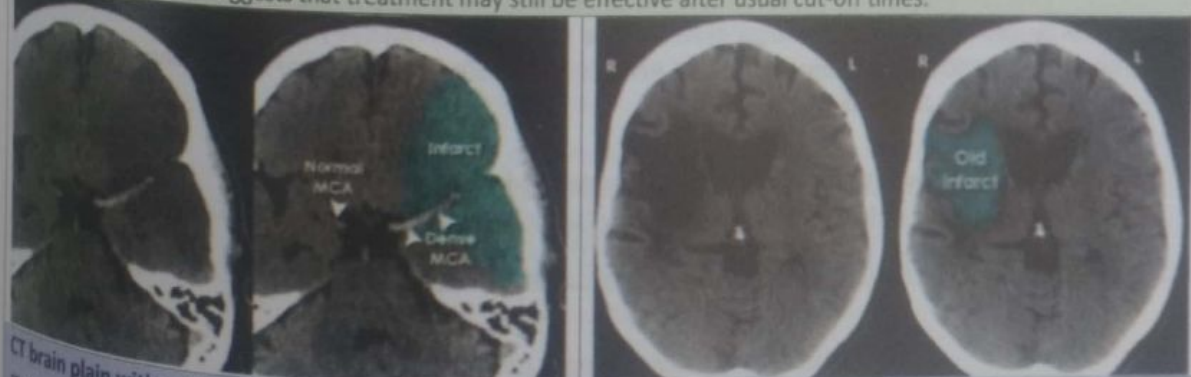


CLINICAL FEATURES

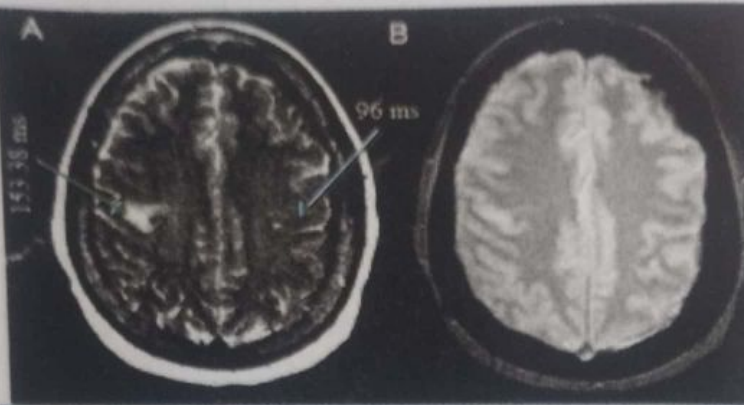
- Sudden onset of focal neurologic deficits: vision loss or visual field defect, weakness, paresthesias, aphasia, ataxia (impaired coordination) and dysarthria
- Nonspecific symptoms: Loss of consciousness, nausea, vomiting, headache, vertigo/dizziness, and seizures.
- Common Stroke Symptoms by Vessel Territory
 - » Anterior Circulation (Carotid Arteries): Weakness or numbness on one side of the face, arm, or leg, difficulty speaking or understanding speech, vision problems in one or both eyes, sudden severe headache.
 - » Middle Cerebral Artery: Weakness or numbness on one side of the body, often affecting the face, arm, and leg, difficulty speaking or understanding speech, confusion, vision disturbances.
 - » Posterior Circulation (Vertebrobasilar Arteries): Severe headache, loss of balance, visual disturbances, difficulty swallowing, dizziness, weakness or numbness on one side of the body, typically affecting the face and limbs.
 - » Vertebral and Basilar Arteries: Difficulty speaking or understanding speech, loss of coordination and balance, visual disturbances, weakness, or numbness on one side of the body, often affecting the face and limbs.
 - » Lacunar stroke: Limb and/or facial weakness (typically affects face, leg, & arm equally), speech difficulty, ataxia, paresthesias or numbness (typically affects face, leg, and arm equally).
- Symptoms suggesting a specific etiology:
 - » Aortic dissection: chest pain, hypotension, dyspnea
 - » Endocarditis: fever, heart murmur
 - » ICH/SAH: sudden, severe headache

DIAGNOSTIC WORKUP

- Initial test: CT brain (without contrast) < MRI (more sensitive for early stroke detection)
- Complete blood count (CBC): may exclude anemia, thrombocytopenia, or polycythemia.
- Blood glucose level: may exclude hypoglycemia or hyperglycemia.
- BUN and creatinine: may exclude acute kidney injury/renal failure.
- Serum electrolytes: may exclude electrolyte disturbance (hyper- or hyponatremia, or hyper- or hypokalemia)
- Liver function tests (LFTs): to assess liver dysfunction.
- Coagulation profile (PT, APTT & INR): may show coagulopathy.
- Additional test for evaluating etiology:
 - » Other tests if indicated: Fasting lipid profile (8-12 hours fasting), HbA1c, Serum TSH and Pregnancy test.
 - » Chest x-ray: if a lung disease is suspected. normal; or cardiomegaly, aortic dissection, pneumonia
 - » ECG: may exclude arrhythmia (atrial fibrillation) or myocardial ischemia.
 - » Cardiac enzyme: Serum troponin – may exclude myocardial infarction.
 - » Electrocardiography: identifies atrial and ventricular thrombus, aortic atheroma, prosthetic valve abnormalities, native valve abnormalities, atrial septal abnormalities, and cardiac tumors.
 - » Lumbar puncture (if SAH suspected and CT brain negative for blood).
 - » EEG, if seizure is suspected.
 - » CT angiography (CTA) or MR angiography: identifies arterial occlusion or stenosis.
 - » CT perfusion or MRI perfusion: a mismatch between perfusion and diffusion scans indicates the presence of penumbra and suggests that treatment may still be effective after usual cut-off times.



CT brain plain without IV contrast: hypoattenuation (darkness) of the brain parenchyma; loss of gray matter-white matter differentiation, and sulcal effacement; hyperdensity in an artery is indicative of a possible thrombosis



MRI imaging

(A) T2-weighted MRI image showing hyperintense signal representing prolonged T2. Shows abnormal T2 of 153.38 ms on the left, compared with the normal contralateral side (96 ms). Note that the lesion is located on the ascending frontal gyrus.
(B) Gradient echo images detect hemosiderin compounds due to magnetic susceptibility of iron. In this case the result is negative



TREATMENT OF ISCHEMIC STROKE (CEREBRAL INFARCTION/CVA) – OUTPATIENT (OPD) (For Acute CVA management – see Emergency chapter)

- ☛ Lifestyle changes (Mediterranean diet, aerobic exercise) & reduction of risk factors (as above mentioned above)
 - ☛ ASCVD Prevention: Hypertension control, diabetes control, high statins therapy and long-term antiplatelet therapy
 - ☛ Monitor, identify and treat any complications.
 - ☛ Provide early rehabilitation and mobilization.
1. Treatment of hypertension – see Hypertension, Cardiovascular medicine chapter.
 - ☛ Tab. Lisinopril 5mg or 10mg (Zestril) x OD, **Dosage:** Initial oral dose 5mg upto 10mg x once daily
 - ☛ OR Tab. Losartan 50mg or 100mg (Eziday, Cozaar) x OD, **Dosage:** Initial oral dose 50mg x once daily
 - ☛ OR Tab. Amlodipine + Valsartan (Newday, Avsar)
 - » **Dosage:** Initially one tab. Newday 5/80mg x OD
 - » **Strength available:** 5/80mg, 5/160mg, 10/160mg
 2. Treatment of diabetes if diabetic – see DM, endocrinology chapter.
 3. High intensity statin therapy:
 - ☛ Tab. Atorvastatin 40mg (Lipitor, Lipiget) x OD, **Dosage:** 40mg up to 80mg x once daily (OD)
 - ☛ OR Tab. Rosuvastatin 20mg (X-Plended, Rovista) x OD, **Dosage:** 20mg up to 40mg x once daily (OD)
 4. Anti-platelets therapy: Tab. Aspirin 75mg, 150mg (Loprin, Ascard) x 0 – 0 – 1 (OD), **Dosage:** 75mg to 150mg x OD
 - ☛ OR Tab. Clopidogrel 75mg (Lowplat, Clopid, Noclot) x 0 – 0 – 1 (OD)
 - ☛ OR Tab. Clopidogrel 75mg + Aspirin 75mg (Ascard plus, Lowplat Plus) 0 – 0 – 1 (Once daily)
 - ☛ OR Tab. Ticagrelor 90mg (Brilinta, Anplag) at loading dose 180mg (2 Tab) x stat on day-1, then 90mg x BD
 - ❖ **N.B. Patients who cannot tolerate aspirin or have aspirin insensitivity OR serious adverse effects → Clopidogrel**
 5. Gastroprotective: may be considered in some cases, routine use in all patients may not be warranted.
 - ☛ Tab. Pantoprazole 40mg (Zopent, Protium, Zentro) x 1 – 0 – 0 (OD) **ایک گولی روزانہ ایک بار کھاتے سے 30 منٹ پہلے**
 6. Screen for depression: Mostly patients get depressed and panic due to brain injury.
 - ☛ Tab. Sertraline 50mg OR 100mg (Zoloft, Sert, Reline) x Initially 50mg, titrated up to 100mg x once daily after breakfast **(ایک گولی دن میں ایک بار ناشتے کے بعد)**
 7. Patient with agitation, anxiety, disturbance of sleep pattern, advice for short term
 - ☛ Tab. Lorazepam 1mg (Ativan) OR Alprazolam 0.5mg (Alp) x 0 – 0 – 1 (HS) **ایک گولی روزانہ رات کو سوتے وقت**

POST-HERPETIC NEURALGIA (PHN)

Post herpetic neuralgia is the most common long-term complication of varicella-zoster virus (VZV) reactivation.

Pathophysiology

- **Primary infection (chickenpox):** Respiratory transmission → VZV inoculates the lymphoid tissue of the nasopharynx and, subsequently, regional lymphoid tissue → viremia and chickenpox → Recovery from chickenpox, but virus remains dormant in dorsal root ganglia (unless reactivated → Recurrent infection)
- **Reactivation (shingles):** VZV reactivated, often many years after the primary infection (e.g., especially in immunocompromised individuals) → Virus replicates in the dorsal root ganglia → Travels through peripheral sensory nerves to the skin → Shingles (less contagious than primary infection)
- **The hallmark of PHN is a lancinating/burning pain in a unilateral dermatomal pattern that persists for three or more months after the onset of herpes zoster (HZ) outbreak.**

△ Post-Herpetic Neuralgia (PHN)

C/C:

- The main symptom of post-herpetic neuralgia is intermittent or continuous nerve pain in an area of your skin previously affected by shingles.
- The pain may come and go or be continuous. It can be described as burning, stabbing, shooting, aching, throbbing or like electric shocks.
- Other symptoms and sensory changes may be present in the same dermatome as the pain:
 - Itch
 - Anaesthesia (numbness)
 - Hyperaesthesia (sensitivity to touch)
 - Allodynia (pain from a light touch)
 - Other sensory change such as reaction to temperature.
- **Motor dysfunction (this is rare):**
 - Autonomic dysfunction (e.g. sweating)
 - Organ damage (e.g. blindness if there is ophthalmic involvement)

Duration of symptoms > 3 months but can persist for years

Rx

Prescription #1

1. **Capsaicin cream** (Capcidol, Zostrix)
OR **Lidocaine Gel** (Xylocaine)
Apply to affected area three to five times daily.
 2. **Tab. Carbamazepine 200mg** (Tegral, Teril, Seizunil)
Dosage: 100mg orally at bedtime; increase dosage by 100mg every 3 days until dosage is 200 mg three times daily or response is adequate (Ref: aafp guidelines)
OR **Cap. Gabapentin 100mg or 300mg** (Gabix, Neogab)
Dosage: 100 to 300 mg orally at bedtime; increase dosage by 100 to 300mg every 3 days until dosage is 300 to 900mg three times daily or response is adequate.
 3. **Tab. Amitriptyline 25mg** (Tryptanol, Amyline, Amitin)
OR **Tab. Nortriptyline 25mg** (Sensival)
Dosage: 25mg orally at bedtime; increase dosage by 25mg every 2 to 4 weeks twice weekly, until response is adequate.
Maximum dose: Titrated up to 150mg per day
- ☞ **Consider Opioids: If Severe neuropathic pain**
Tab. Tramadol 100mg (Tramal SR, Tonoflex SR) x BD/TDS
OR **Tab. Tapentadol 75mg** (Tapento IR, Tydel) x BD

Rx

Prescription #2

1. **Cap. Pregablin 75mg, 100mg** (Gabica, Zeegap, Syngab)
Dosage: Start with 75 mg twice a day for 3–7 days. If required, increase dose to 150 mg twice a day after 3–7 days, to a maximum of 300 mg twice a day after another 7 days.
2. **Tab. Naproxen sodium 500mg** (Flexin, Neoprox)
1 – 0 – 1 (BD)
3. **Tab. Nortriptyline 25mg** (Sensival)
Dosage: 25mg orally at bedtime; increase dosage by 25mg every 2 to 4 weeks until response is adequate.
4. **Cap. Esomeprazole 40mg** (Nexum, Esso)
0 – 0 – 1 (OD) ایک گولی روزانہ ایک بار کھاتے سے 30 منٹ پہلے



TRIGEMINAL NEURALGIA (5TH CN PALSY)

△ Trigeminal neuralgia (چہرے کا اعصابی درد)

Clinical features

- ✦ **Unilateral facial pain:** paroxysmal, severe shooting or stabbing (like an electric shock), followed by a burning ache
 - ↳ Lasts several seconds (in rare cases, several minutes) and may occur up to 100 times/day
 - ↳ Typically shoots from mouth to the angle of the jaw on the affected side
 - ↳ Occurs either at rest or is triggered by movements such as chewing, talking, or touch (e.g., brushing teeth, washing face); becomes worse with stimulation
- ✦ **Facial spasms may occur.**
- ✦ **Psychological distress:** ranging from dysphoria to severe depression with suicidal tendencies
- ✦ **Usually progressive course**

Diagnostic workup

Trigeminal neuralgia is a clinical diagnosis.
MRI should be performed to R/O other causes

Diagnostic criteria

All below criteria must be fulfilled:

- Recurring unilateral face pain in the area innervated by one or more divisions of the trigeminal nerve
- **Pain characteristics**
 - Severe
 - Lasting no more than two minutes
 - **Quality:** sharp, shooting, stabbing, or electric shock-like
- **Triggered by innocuous stimuli** in the area innervated by the affected trigeminal nerve divisions
- Another ICDH-3 diagnosis does not better explain the symptoms.

Rx

Prescribe ONE of the following

- ✦ **Tab. Carbamazepine 200mg** (Seizunil, Tegrol, Terol)
Dosage: Initially 200mg x BD, titrated up to 400mg x BD
Maximum dosage: 400 to 1600mg/24 hours
(Oxalepsy, Telox, Trioptal)
- ✦ **OR Tab. Oxcarbazepine 150mg, 300mg, 600mg**
Dosage: Initially 50 or 75mg x BD, up to 150mg x BD
Maximum dose: 150 to 300mg/24hours
- ✦ **OR Cap. Pregablin 50mg, 75mg, 150mg** (Gabica, Zeegap)
Dosage: Initially 50 or 75mg x BD, up to 150mg x BD
Maximum dose: 150 to 300mg/24hours
- ✦ **OR Cap. Gabapentin 300mg** (Gabix, Neogab, Gaba)
Dosage: Initially 300mg x BD/TDS
Maximum dose: 900mg to 3600mg/24hours
- ✦ **OR Tab. Baclofen 10mg** (Baclast, Lioresal, Baclin)
Dosage: 10 to 20mg orally three to four times.
- ✦ **OR Tab. Topiramate 25mg or 50mg** (Hitop, Topamax)
Dosage: start initially 25mg once at night titrated weekly by 25mg x twice daily, titrated up to 200mg
Maximum dose: 400mg/day
- ✦ **OR Tab. Lamotrigine 50mg or 100mg** (Lamictal, Lamonil)
Dosage: 100mg to 500mg orally daily

Rx

Prescription # 2

1. **Tab. Oxcarbazepine 150mg, 300mg, 600mg**
Dosage: Initially 50 or 75mg x BD, up to 150mg x BD
Maximum dose: 150 to 300mg/24hours
2. **Tab. Naproxen sodium 250mg or 500mg** (Flexin, Proxen)
Dosage: 250mg to 500mg x two times a day x 1-2 week
3. **Cap. Esomeprazole 40mg** (Eskem, Esso)
0-0-1 (OD) for 1-2 week
ایک گولی روزانہ ایک بار کھانے سے 30 منٹ پہلے

BELL'S PALSY (FACIAL NERVE PARESIS/7TH CN PARALYSIS)

Definition: Bell palsy (In Urdu "LAQWA = لغوه") is an idiopathic facial paresis of lower motor neuron type that has been attributed to an inflammatory reaction involving the facial nerve near the stylomastoid foramen or in the bony facial canal.

Etiology

Idiopathic (most common cause of peripheral facial nerve palsy): Acute idiopathic peripheral facial palsy

Secondary causes/Risk factors:

- » Trauma (e.g., temporal bone fracture)
- » **Infection:** Herpes zoster (Ramsay Hunt syndrome), Borreliosis (Lyme disease), HSV reactivation, HIV, Malignant otitis externa, Influenza virus (due to intranasal influenza vaccine) and URTI
- » **Tumors** (parotid gland tumors, acoustic neuroma)
- » **Other risk factors include:** Pregnancy, Diabetes mellitus, Hypertension, Guillain-Barré syndrome (GBS), Sarcoidosis (Heerfordt syndrome), Amyloidosis, dental procedures and Stroke

Clinical features

1. Central vs. peripheral facial nerve palsy

Motor signs in central and peripheral facial palsy

Clinical feature	Central (signs are contralateral to the lesion)	Peripheral (signs are ipsilateral to the lesion)
Ability to frown or lift eyebrows	Intact	Impaired
Ability to close the eyelids completely	Intact	Impaired
Mouth drooping	Present	Present

2. Additional signs of peripheral facial palsy

- » **Sensory disturbances**
 - » **Pain:** Painful sensation around (Postauricular pain) or behind the ear or otalgia
 - » Impairment of taste in the anterior tongue
 - » Hyperacusis (unusual sensitivity to sound on the same side as the facial palsy)
- » **Dry mouth** (as a result of decreased saliva production)
- » **Ocular features**
 - » **Bell's phenomenon:** a physiologic, reflexive movement of the eye (upward and outward) that occurs when the eyelid is actively closed
 - » **Lagophthalmos:** The patient cannot fully close the eyes due to paralysis of the orbicular oculi muscle
 - » Decreased lacrimation
 - » Keratoconjunctivitis sicca (dry eye)
 - » **Corneal ulceration and keratitis** (inflammation of the cornea and is characterized by corneal edema, infiltration of inflammatory cells, and ciliary congestion)
 - » **Ectropion:** where the lower eyelid droops away from the eye and turns outwards
- » **Facial synkinesis:** involuntary movements of the facial muscles (facial spasms while closing the eyes)

Diagnostic workup

- » **Clinical diagnosis of exclusion,** based on history and physical examination alone → acute, unilateral facial palsy, with an otherwise normal physical examination.
- » **Medical history**
 - » **Ask about symptom onset and duration** (e.g., acute vs. progressive).
 - » **Assess for possible secondary causes** as mentioned above, e.g., stroke, tumors, recent infections, and exposure from outdoor trips.
- » **Physical examination**
 - » **Evaluate facial asymmetry at rest.**
 - » **Ask the patient to perform facial movements.**
 - Assess for asymmetries and facial muscle strength.
 - Differentiate between motor signs in central and peripheral facial palsy.
 - » **Perform a complete neurological examination:** Look for focal neurological signs.
 - » **Evaluate for signs indicative of a secondary cause,** e.g., shingles, herpes zoster oticus, erythema migrans, tick bites, signs of trauma.

- Investigation: INVESTIGATIONS ARE NOT ROUTINELY needed for acute unilateral facial nerve palsy unless a secondary cause is suspected, based on atypical symptoms and/or abnormal physical examination findings.
- Referral to specialist consultation is advised.
 - » **Laboratory test:** Consider selecting infectious causes.
 - **Varicella zoster virus (VZV):** e.g., PCR or serological studies
 - **Lyme disease:** e.g., ELISA IgM and IgG antibodies for *Borrelia*, Western blot
 - » **Electroneurography (ENoG) or Evoked electromyography:**
 - ↳ Indicated in acute cases where physical exam demonstrates complete facial paralysis. Should be performed no sooner than 72 hours to allow for Wallerian degeneration to occur and no later than 14 days following the onset of palsy. Typically performed using skin surface electrodes.
 - ↳ **Finding:** >90% decrease in the amplitude of compound muscle action potential (CMAP) on the affected compared with the healthy side is an indication for confirmatory needle electromyography
 - » **CT scan** (fine-cut, non-enhanced): normal or may reveal tumor
 - » **MRI** (Gadolinium-enhanced fine-cut of facial nerve course): MRI is the method of choice and is most useful for excluding other causes (neoplastic, vascular, or traumatic) of facial nerve palsy.



TREATMENT OF BELL'S PALSY (FACIAL NERVE PALSY)

Symptomatic therapy

- Provide symptom-based treatment for all patients (regardless of the cause).
- Initiate eye protection: artificial tears, eye lubricant drops/ointment, and/or taping or patching of the eye
- Incomplete mouth closure: Advise the patient on proper lip and mouth care.
- Persistent facial nerve paresis (≥ 3 months): Consider physical therapy and facial reconstructive options.

Targeted treatment

- Idiopathic facial nerve palsy is self-limited, approximately 60% recover completely without treatment but early treatment is recommended with corticosteroids to increase the chance of complete recovery.
- Begin initial management of ischemic stroke without delay if acute central facial nerve palsy is suspected.
- Oral corticosteroids: Consider for all patients (regardless of severity) within 48–72 hours of symptom onset
 - ↳ **Tab. Prednisolone 5mg** (Deltacortril, Rapicort) at dose 50 mg per orally daily for 10 days
5 – 0 – 5 (5 tablets = 25mg) OR 50mg orally once daily (OD) for 5 days, then 40mg OD for 1 day, then 30mg OD for 1 day, then 20mg OD for 1 day, then 10mg OD for 1 day, then 5mg OD for 1 day, then stop
- Adjuvant: Consider adding an antiviral to steroid therapy, if there is evidence of herpetic vesicles in the external ear canal. (Do not use antiviral as monotherapy).
 - ↳ **Tab. Aciclovir 400mg** (Acylex, Aclova, Zovirox) at dose 400mg orally 5 times daily for 10 days OR 800mg (Tab. Acylex OR Tab. Santovir OR Tab. Aclova) x 3 times daily for 5–10 days
 - ↳ **OR Tab. Valacyclovir 500mg** (Valtrex) x orally, twice daily for 5–7 days
- Tab. Methycobalamin 500mcg** (Incobal, Neuromet) x orally, twice daily for 10–14 days
- For secondary facial nerve palsy treatment of underlying cause or refer to sub-specialty
- Follow up with specialist consult and/or advanced studies, if the patient has any of the following:
 - » No signs of improvement in 2–3 weeks
 - » Persistent (≥ 3 months), progressive, and/or recurrent symptoms



Right sided facial nerve paralysis

Inability to wrinkle brow

Drooping eyelid;
inability to close eye

Inability to puff cheek;
asymmetrical smile

Drooping corner of mouth;
dry mouth



PARKINSON'S DISEASE (PD)

Clinical features

- ✓ Signs of PD gradually progress over time: The clinical course is usually > 10 years; unilateral onset with persistently asymmetrical course (i.e. unilaterally pronounced symptoms) but may progress to the contralateral side
- ✓ Parkinsonism
 1. Bradykinesia/akinesia: Slowed movements in combination with decreased amplitude/speed when moving
 2. Resting tremor (4–6 Hz)
 - » Pill-rolling tremor that subsides with voluntary movements but increases with stress
 - » Most common in the hands but may involve the legs, jaw, lips, and tongue
 3. Rigidity: increased and persistent resistance to **passive** joint movement that is independent of speed
 - » **Froment maneuver**: The patient is asked to perform repetitive movements in the contralateral extremity (E.g., opening and closing of the left fist if the right side is examined) → Subclinical rigidity becomes more pronounced and may be detected.
 - » **Cogwheel rigidity**: A phenomenon caused by the overlay of increased muscle tonus and resting tremor in patients with Parkinson disease. May manifest before tremor becomes clinically apparent
 - Muscles in an extremity (most commonly the arms) are passively stretched, eliciting a jerking-like motion.
 - Muscle tone should be tested with at least two joints.
- ✓ Postural instability: Imbalance and tendency to fall → evaluate with the pull test
- ✓ Parkinsonian gait: shuffling gait with quickened and shortened steps
- ✓ Freezing: sudden inability to start or continue movements
- ✓ Festination: gait pattern characterized by small, increasingly quick steps
- ✓ Unhabituated glabellar reflex
- ✓ Signs of dystonia: after raising the patient's head and suddenly releasing it, it sinks back down very slowly.
- ✓ Pyramidal signs (but normal tendon reflexes)
- ✓ Micrographia: size of handwriting is reduced
- ✓ Hypomimia: low degree of facial expression
- ✓ Other clinical features
 - » Early features: Prodromal PD and/or Lewy body dementia: rapid eye movement sleep behavior disorder (RBD)
 - **Sensory**: Hyposmia or anosmia (potential early symptom), Dysesthesias: muscle and joint pain (often in the shoulder/arm region)
 - **Motor**: reduced swinging of arms while walking
 - **Personality changes**: e.g., withdrawal, apathy
 - » Late features:
 - **Motor**
 - **Freezing**: sudden inability to start or continue movements (e.g., while walking)
 - **Propulsion**: forward-leaning gait with risk of patient falling forward
 - **Micrographia**: size of handwriting is reduced
 - Low degree of facial expression (hypomimia), decreased blinking
 - **Autonomic**: Depression, dementia

Diagnostic workup

- ✓ Parkinson disease is a clinical diagnosis!
- ✓ MRI is usually used to rule out other possible causes of parkinsonism (E.g., strokes, tumors)

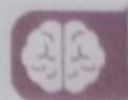
Treatment

To date, there is no cure for Parkinson disease. Treatment is aimed at relieving symptoms and should generally begin once patients develop significant functional disability

- ✓ General measures: Physiotherapy, Speech and language therapy, Occupational therapy, Support groups

Medication:

- » **First line treatment for the patients age > 65 or multimorbid patients of any age**: Levodopa + Carbidopa
- » **First line treatment for the patients age < 65 with no significant comorbidities**
 - **Ropinirole (Requip)**: as monotherapy OR in combination with levodopa/carbidopa
 - **Selegiline (Selgin 5mg)**: may be used alone or combine with dopamine agonists or Levodopa + Carbidopa
 - **Entacapone (COMT inhibitors) in combination with Levodopa+Carbidopa**: Paridopa (Pharmevio)
- » **Alternatives**: Carbidopa+ Levodopa (Sinemet/Neudopa), bromocriptine, Amantadine (used to reduce levodopa-induced dyskinesias), Bzotroprine, Trihexyphenidyl.



△ Parkinson's Disease C/C:

- » Tremor
- » Rigidity
- » Akinesia
- » Postural instability
- » Mnemonic as TRAP

Associated conditions

1. Dementia
2. Depression
3. Sleep disorders
4. Psychosis

Treatment of associated symptoms

Depressive moods:

- » SSRIs: Escitalopram (Estar, Morcet)
- » SNRIs: venlafaxine (Efexor, Vendep)

Dementia: Donepezil (Doncept, Alzex)

Psychotic episodes: Olanzapine (Olanzia, Olepra), Quetiapine (Qusel)

Dyskinesias: Procyclidine (Kamadrin), Trihexyphenidyl (Hexidyl 2mg)

Levodopa + Carbidopa + Entacapone

- **Brand:** Dopacone, Paridopa, Cabilov and stalevo
- The optimum daily dose must be determined by careful titration of levodopa in each patient.
- The daily dose should be preferably optimised using one of the seven available tablet strengths:
levodopa/carbidopa/entacapone
 - » 50mg/12.5mg/200mg
 - » 75mg/18.75mg/200mg
 - » 100mg/25mg/200mg,
 - » 125mg/31.25mg/200mg
 - » 150mg/37.5mg/200mg,
 - » 175mg/43.75mg/200mg
 - » 200mg/50mg/200mg

Rx

Patients the age > 65 or multimorbid patients of any age

1. **Tab. Carbidopa PLUS Levodopa** (Sinemet, Neudopa)
 $\frac{1}{2} - \frac{1}{2} - \frac{1}{2}$ (Rx should start from gradually low dose to high)
Levodopa is best taken between meals (e.g., 30 minutes before a meal)
2. **Tab. Procyclidine 5mg** (Kamadrin, Kampro)
 $\frac{1}{2} - 0 - \frac{1}{2}$, (2.5mg = Half x BD), than I - 0 - I (BD)

If Tremors not controlled & still tremors then add on

3. **Tab. Amantadine 100mg** (PK Merz, Amanta)
Initially 100mg x OD, than 100mg x 2-3 time per day

Rx

Patients under the age of 65 with no significant comorbidities

1. **Tab Ropinirole 0.25mg, 1mg, 2mg** (Ronirol, Requip, Ropinol)

Week	Ascending Dosage	Total Daily Dose
1	0.25 mg x TDS	0.75 mg
2	0.5 mg x TDS	1.5 mg
3	0.75 mg x TDS	2.25 mg
4	1 mg x TDS	3 mg

- » After Week 4, if necessary, the daily dose may be increased by 1.5mg/day on a weekly basis up to a dose of 9mg/day, and then by up to 3mg/day weekly up to a maximum recommended daily dose of 24mg/day (8 mg three times daily).
- » Ropinirole should be discontinued gradually over a 7-day period in patients with Parkinson's disease.
- » The frequency of administration should be reduced from three times daily to twice daily for 4 days. For the remaining 3 days, the frequency should be reduced to once daily prior to complete withdrawal of Ropinirole

Give ropinirole single drug if not respond PLUS add on

2. **Tab. Carbidopa + Levodopa** (Sinemet, Neudopa)
 $\frac{1}{2} - \frac{1}{2} - \frac{1}{2}$ (Rx should start from gradually low dose to high)
3. **Tab. Procyclidine 5mg** (Kamadrin, Kampro)
 $\frac{1}{2} - 0 - \frac{1}{2}$, (2.5mg = Half x BD), than I - 0 - I (BD)

Rx

Patients under the age of 65 with no significant comorbidities

1. **Tab. Levodopa+ Carbidopa +Entacapone** (Dopacone, Paridopa)
 2. **Tab Procyclidine 5mg** (Kamadrin, Kampro)
 $\frac{1}{2} - 0 - \frac{1}{2}$, (2.5mg = Half x BD), than I - 0 - I (BD)
- If Tremors not controlled & still tremors then add on
3. **Tab Amantadine 100mg** (PK Merz, Amanta)
Initially 100mg x OD, than 100mg x 2-3 time per day

RESTING TREMOR

Name: _____ Age: _____ Sex: _____ Date: _____
 Temperature: _____ B.P.: _____ Pulse: _____ Resp. Rate: _____

- Definition: Resting tremor occurs when a body part is at complete rest against gravity. Tremor amplitude decreases or disappears with onset of movements (voluntary activity), but once partial stability is attained in a new position, the tremors returns.
- Age of onset: ~ 60 years
- Etiology
 - » Parkinson disease
 - » Drug induced parkinsonism (neuroleptics, metoclopramide)
 - » Progressive supranuclear palsy
- Pathophysiology: caused by a dysfunction of the basal ganglia, especially substantia nigra

△ Resting tremor

C/C:

- » Typically, asymmetric resting tremor of the extremities (especially apparent in the hands); at a low frequency (4–6 Hz, rarely up to 9 Hz)
- » “Pill-rolling” of hands that subsides with voluntary movements.
- » Reduced with target-directed movement
- » In early Parkinson disease, unilateral tremors are common.
- » Worsens with emotional stress
- » Often associated with rigidity, bradykinesia, and postural instability (also see “Parkinson disease”)

Diagnostics

- » Typically a clinical diagnosis
- » MRI for atypical presentations
- » The history and examination of the patient with tremor should focus on 3 practical questions:
 1. Is the movement disorder actually tremor?
 2. Is the tremor isolated, or are there accompanying neurologic abnormalities?
 3. What are the phenomenologic features of the tremor?

TREATMENT SIMILAR AS PARKINSONS DISEASE

Rx

Patients the age > 65 or multimorbid patients of any age

1. **Tab. Carbidopa PLUS Levodopa** (Sinemet, Neudopa)
 $\frac{1}{2} - \frac{1}{2} - \frac{1}{2}$ (Rx should start from gradually low dose to high)
 Levodopa is best taken between meals (e.g., 30 minutes before a meal)
2. **Tab. Procyclidine 5mg** (Kamadrin, Kampro)
 $\frac{1}{2} - 0 - \frac{1}{2}$, (2.5mg = Half x BD), than 1 – 0 – 1 (BD)
 If Tremors not controlled & still tremors then add on
3. **Tab. Amantadine 100mg** (PK Merz, Amanta)
 Initially 100mg x OD, than 100mg x 2-3 time per day

Rx

Patients under the age of 65 with no significant comorbidities

1. **Tab Ropinirole 0.25mg, 1mg, 2mg** (Ronirol, Requip, Ropinol)

Week	Ascending Dosage	Total Daily Dose
1	0.25 mg x TDS	0.75 mg
2	0.5 mg x TDS	1.5 mg
3	0.75 mg x TDS	2.25 mg
4	1 mg x TDS	3 mg

- » After Week 4, if necessary, the daily dose may be increased by 1.5mg/day on a weekly basis up to a dose of 9mg/day, and then by up to 3mg/day weekly up to a maximum recommended daily dose of 24mg/day (8 mg three times daily).
- » Ropinirole should be discontinued gradually over a 7-day period in patients with Parkinson's disease.
- » The frequency of administration should be reduced from three times daily to twice daily for 4 days. For the remaining 3 days, the frequency should be reduced to once daily prior to complete withdrawal of Ropinirole

Give ropinirole single drug if not respond PLUS add on

2. **Tab. Carbidopa + Levodopa** (Sinemet, Neudopa)
 $\frac{1}{2} - \frac{1}{2} - \frac{1}{2}$ (Rx should start from gradually low dose to high)
3. **Tab. Procyclidine 5mg** (Kamadrin, Kampro)
 $\frac{1}{2} - 0 - \frac{1}{2}$, (2.5mg = Half x BD), than 1 – 0 – 1 (BD)



ESSENTIAL TREMOR

Name: _____ Age: _____ Sex: _____ Date: _____
 Temperature: _____ B.P: _____ Pulse: _____ Resp. Rate: _____

☞ **Definition:** Essential tremor (ET) is a progressive, neurological disease characterized by tremor, most often of the hands or arms. A tremor is an involuntary, rhythmic, movement of a body part.

☞ **Epidemiology**

» Most common form of tremor

» **Bimodal distribution:** teens and 6th decade of life (common in elderly patients)

☞ **Etiology:** positive family history (50–70%; autosomal dominant inheritance) or sporadic; benign form

△ **Essential tremor**

C/C:

- » **Localization:** hands; (= 90%), head (= 30%; "yes-yes" or "no-no" motion), voice (=15%)
- » Mostly bilateral postural tremor with a frequency of 5–10 Hz
 - Slowly progressive
 - Worse with sustained voluntary movement, stress or anxiety, fatigue, and caffeine
 - Improves with alcohol consumption
- » The essential tremor may be accompanied by an intention tremor and/or a resting tremor
- » Consider an essential tremor in a patient presenting with chronic bilateral hand tremors without further neurological deficits and positive family history.

Diagnostic workup

- » usually a clinical diagnosis of exclusion
- » The history and examination of the patient with tremor should focus on 3 practical questions:
 1. Is the movement disorder actually tremor?
 2. Is the tremor isolated, or are there accompanying neurologic abnormalities?
 3. What are the phenomenologic features of the tremor?

In drug-resistant cases

- ☞ Deep brain stimulation (DBS)
- ☞ Thalamotomy

Rx

☞ **Drug of choice:** Propranolol or Primidone

☞ **Alternatives** (if Propranolol and Primidone are unresponsive or contraindicated)

- » **Beta blockers:** Atenolol, Nadolol
- » **Anticonvulsants:** Gabapentin, topiramate
- » **Benzodiazepines:** Alprazolam, clonazepam

1. **Tab. Propranolol 10mg OR 40mg** (Inderal, Cardinal)

- » **Dosage:** starting dose is 20mg to 40mg twice daily, increasing the dose according to the patient response
- » **Therapeutic dose:** 120mg to ≤320 mg/day

OR **Tab. Primidone 250mg** (Mysoline)

- » **Dosage:** starting in a low dose of 25 to 62.5mg at night and increasing to 250mg (Maximum: 750mg/day)

2. **±Tab. Alprazolam 0.5mg or 1mg** (Alp, Xanax, Praz)OR **Tab. Clonazepam 0.5mg or 2mg** (Revotril, Naze)

- » **Dosage:** starting dose 0.25 to 0.5mg at night
- » **Therapeutic dose:** 0.25mg to 3mg/day

ALTERNATIVES AGENT:☞ **Tab. Atenolol 25mg, 50mg, 100mg** (Tenormin, Normitab)

- » **Dosage:** starting dose is 25mg to 50mg per day
- » **Therapeutic dose:** 50mg to 200mg/day

☞ **Tab. Topiramate 25mg, 50mg, 100mg** (Hitop, Topiro, Topagen)

- » **Dosage:** starting dose is 25mg to 50mg per day at bedtime or at 2 divided doses, titrated up to 200mg/day
- » **Therapeutic dose:** 200mg to ≤400 mg/day.

☞ **Cap. Gabapentin 100mg, 300mg, 400mg** (Gabix, Neogab, Gabal)

- » **Dosage:** starting dose is 300mg/day in 3 divided doses, increasing up to 1200mg per day in 3 divided doses
- » **Therapeutic dose:** 1200mg to 1800 mg/day

ALZHEIMER'S DISEASE (AD)

Etiology

Genetic factors:

- **Amyloid precursor protein (APP):** Gene – Linked with early-onset familial AD (10-15% in cases), APP gene is located on chromosome 21 (Increased risk of early-onset AD due to APP. Overexpression), median age is 49 years
- **Presenilin-1 (PSEN1):** Gene – linked with early-onset familial AD (~50% in cases), due to mutations of other genes, median age is ~43 years.
- **Presenilin-2 (PSEN2):** Genetic mutations cause the rarest form of familial AD. Later onset (average = 54 years)
- **Apolipoprotein E (Apo E):** Risk of late-onset AD ↑ with the number of carried Apo E4 alleles. Apo E2 alleles may have a protective effect (↓ the risk of late-onset sporadic AD). Apo E3 alleles neither ↓ nor ↑ risk of developing AD

Other risk factors

- Age (strongest predisposing factor for regular AD)
- Family history of dementia (strongest predisposing factor for early-onset AD)
- Low socioeconomic and/or educational status
- Diabetes, obesity, dyslipidemia
- Hypertension, peripheral atherosclerosis, and CVS disease
- African American or Hispanic descent (compared to White individuals)
- Lack of physical activity (independent risk factor)
- Traumatic brain injuries
- Environmental factors (e.g., secondhand smoke)
- Sleep deprivation

Pathophysiology

The following pathophysiological mechanisms contribute to Alzheimer's Disease (AD):

- **Senile plaques (neuritic plaques):** Extracellular plaques located in the grey matter of the brain, Aβ protein is the main component of the plaques. Enzymatic cleavage of transmembranous APP by β-secretase and γ-secretase → Aβ peptide aggregation → formation of insoluble plaques → neurotoxic effect
- **Neurofibrillary tangles:** Intracellular Tangles are composed of hyperphosphorylated tau protein (an insoluble microtubule-associated protein). Increased phosphorylation (hyperphosphorylation) of tau → formation of intracellular fibrils → neurotoxic effect (number of tangles correlates with the degree of cognitive impairment)
- **Reduced cholinergic function:** Acetylcholine deficiency is related to the degeneration of cholinergic neurons and likely plays a role in the decline of cognitive abilities.

Diagnostic approach

- Consider AD in patients with dementia or mild neurocognitive disorder.
- Establish the diagnosis based on clinical criteria and neuropsychological testing.
- Consider advanced testing in consultation with neurology: Biomarkers (PET scan or CSF), Electroencephalogram (EEG), and Testing for genetic factors in Alzheimer disease
- A definitive diagnosis requires neuro-histopathological confirmation (not usually done).

Diagnostic criteria for Alzheimer disease

DSM-5 diagnostic criteria for major neurocognitive disorder due to Alzheimer disease

	Probable major neurocognitive disorder due to AD	Possible major neurocognitive disorder due to AD
	• Diagnostic criteria for major neurocognitive disorders are fulfilled. • Insidious onset with gradually progressive symptoms in ≥2 cognitive domains	
Criteria	• All of the following: » Objective impairment in learning and memory and ≥ 1 other cognitive domain » Steady cognitive decline with no plateaus » No evidence of other causes • OR evidence of a causative genetic mutation	Absence of any features indicating probable AD

• **MRI brain:** Indicated in all patients as part of the initial evaluation of major neurocognitive disorder

Supportive findings

- **Signs of generalized or focal cerebral atrophy:** Enlarged ventricles (ventriculomegaly), Narrowing of gyri and prominent cerebral sulci (hydrocephalus ex vacuo)
- Disproportionate atrophy of the medial temporal lobe including the hippocampi, amygdala, cingulate cortex, and parahippocampal gyrus
- **PET Scan:** FDG-PET (↓ glucose metabolism in temporal and parietal cortices), Amyloid-β (Aβ)-PET (↑ amyloid uptake signal), Tau-PET (prognosis based assessment ↑ tau uptake signal in temporal and parietal cortices)
- **Other investigations:** CSF analysis (↑ Phospho-tau protein, ↓ Aβ proteins Aβ 1-42), Electroencephalogram (EEG)



Management of Alzheimer's Disease (AD)

1. Lifestyle modifications:

- Adhering to a regular sleep schedule
- Maintaining a familiar environment/maintaining active role in the family and community is beneficial
- Removing ambient noise
- Aerobic exercise (running, swimming, walking, hiking, aerobics classes, dancing) – for 30 minutes several days per week) may reduce the rate of functional decline and decrease the patient's caregiving needs and may reduce the risk of dementia in normal individuals.

2. Cognitive rehabilitation: memory training (e.g., puzzles, interactive games) to support memory retention and strategies to compensate for cognitive and functional decline

3. Physical activity: improves physical strength, which slows functional decline

4. Pharmacological treatment of associated symptoms: In patients who have not adequately responded to supportive care, the following classes of drugs may be considered:

- Atypical antipsychotics in patients with agitation, hallucinations, insomnia: Quetiapine, Risperidone
- Anti-depressants (SSRIs) in patients with depression: Escitalopram, citalopram
- Vitamins supplement: Vitamin-E (Evion), B-complex (Neurobion), methylcobalamine (Methycobal)
- Other drugs (Placebo effect) drugs: Ginkgobiloba, Ginseng or combine both

△ Alzheimer's Disease (AD)

C/C:

- The leading cause of dementia
- Early-onset (before the age of 65)
- Most common symptom of AD is short-term memory loss
- Many cognitive functions, including attention control, reasoning, orientation, and language

COGNITIVE FEATURES:

Common symptoms of cognitive impairment

- Short-term memory impairment (insidious onset, slow progress with episodic memory affected first)
- Language impairment
- Temporal and spatial disorientation (patients are usually not oriented to person, place, time, or events)
- Impairment of executive functions and judgment

Less common symptoms:

- Primary progressive aphasia
- Apraxia
- Alexia
- Agnosia
- Acalculia

NON-COGNITIVE FEATURES:

- Behavioral changes: Apathy, Aggression, irritability, and agitation
- Mood disorders (symptoms of depression)
- Anxiety and mutism
- Hallucinations and paranoia
- Hyposmia
- Insomnia
- Urinary incontinence
- Myoclonus
- Seizures

Rx

Mild to moderate Alzheimer's Disease (AD)

General principles

- There is currently no curative therapy for Alzheimer's Disease
- Management should include:
 - Supportive care for dementia
 - Lifestyle modifications
 - Pharmacotherapy for Alzheimer's Disease as indicated
 - Treatment of commonly associated symptoms
- Overall goals: Maintain function, Delay symptom progression

1. Tab. Rivastigmine 1.5mg, or 3mg, 4.5mg or 6mg (Exelon)

Dosage: start at 1.5mg per orally x BD, then increasing every 2 weeks by 1.5mg x BD to a goal of 3mg to 6mg x per orally x BD

OR Tab. Galantamine 8mg or 12mg (Dementio ER)

Dosage: start at 4mg orally BD, then increasing every 4 weeks by 4mg x BD to a goal of 8mg to 12mg extended release (ER) per orally x once daily.

OR Tab. Donepezil 5mg or 10mg (Aricept, Doncept, Donepi)

Dosage: Start at 5mg per orally for 4 weeks, then increase to 10mg once daily.

2. Cap. Vitamin-E 400mg (Evion 400, Zescap 400, Evo-E 400mg) 1-0-1 (BD)

Add in patients with depression features

3. Tab. Escitalopram 5mg or 10mg (Ciprallex, Estar, Citanew) 1-0-0 (OD)

Add in patients with agitation, hallucinations, insomnia

4. Tab. Quetiapine 25mg, or 100mg (Qusel, Seroquel, EvoKalim)

Dosage: start 25 mg orally daily as needed, increasing to three times daily as needed.

OR Tab. Risperidone 1mg or 2mg (Buzon, Risp, Risperdal)

Dosage: start with 0.5 to 1mg x OD, increasing weakly as needed upto 1mg to 2mg twice daily.

5. Syp. Ginkgo biloba/Ginseng (Cogin, Ginbex) 2 teaspoonful x Twice daily

Treatment Guidelines:

- » Insomnia is common, which is treated with
» **Tab. Trazodone 50mg or 100mg** (Deprel, Trazolam) initially at dose 25-50mg orally at bedtime as needed, can be safe & and effective.
- » Antihistamine hypnotics must be avoided, along with Benzodiazepines (Alprazolam, Clonazepam, Lorazepam, Diazepam), because of their tendency to worsen cognition and precipitate delirium.
- » Other prescription hypnotics such as zolpidem may result in similar adverse reactions.
- » Avoid drugs with strong anticholinergic effects (e.g., diphenhydramine).
- » The combination of **Dextromethorphan and Quinidine** (up to 30/10 mg orally twice daily) has shown promise in early clinical trials.

» **A β monoclonal antibody: Aducanumab**

» Indication:

- Mild Alzheimer disease (AD)
- Mild neurocognitive disorder due to AD

» Brand: Aduhelm 170mg/1.7ml (100mg/ml)

Table: Dosing titration schedule

IV Infusion (every 4 week)	Dosing ~1 hour
Infusions 1 and 2	1mg per kg
Infusions 3 and 4	3mg per kg
Infusions 5 and 6	6mg per kg
Infusions 7 and beyond	10mg per kg

Rx

Moderate to severe Alzheimer's Disease (AD)

1. **Tab. Memantine 5mg, 10mg or 20mg** (Ebixa, Rement, Afdol, Demantin, Alzagon)

Dosage: start at 5 mg orally daily, then increase by 5 mg per week up to a target of 10 mg x BD) is approved for the treatment of moderate to severe Alzheimer disease

» **Memantine** often used in combination with donepezil

» **Tab. Donepezil 5mg or 10mg** (Aricept, Doncept, Donep)

» **Dosage:** Start at 5mg per orally for 4 weeks, then increase to 10mg daily (23mg daily dose is approved for moderate to severe Alzheimer disease)

2. **Cap. Vitamin-E 400mg** (Evion 400, Zescap 400, Evo-E 400mg) 1-0-1 (BD)

Add in patients with depression features

3. **Tab. Escitalopram 5mg or 10mg** (Cipralext, Estar, Citanew) 1-0-0 (OD)

Add in patients with agitation, hallucinations, insomnia

4. **Tab. Quetiapine 25mg, or 100mg** (Qusel, Seroquel, EvoKaLm)

» **Dosage:** start 25 mg orally daily as needed, increasing to three times daily as needed.

» **OR Tab. Risperidone 1mg or 2mg** (Buzon, Risp, Risperdal)

» **Dosage:** start with 0.5 to 1mg x OD, increasing weakly as needed upto 1mg to 2mg twice daily.

5. **Syp. Ginkgo biloba/Ginseng** (Cogin, Ginbex) 10ml (2 teaspoonful) x Twice daily

MRI brain (T2-weighted; axial plane) of Alzheimer's Disease (AD)

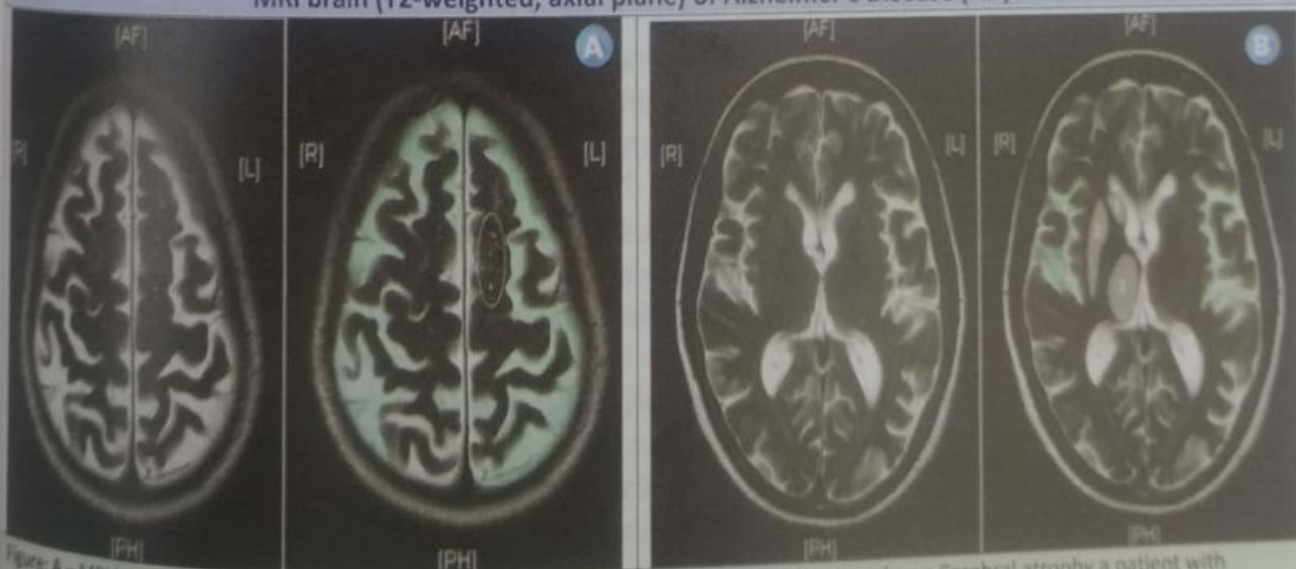


Figure: A – MRI brain – shows cerebral atrophy of a patient with Alzheimer disease with increasing memory disturbance. There is bilateral cerebral atrophy, with prominent sulci (green overlay). Multiple small hyperintense foci in the white matter (examples outlined) are enlarged perivascular spaces (Virchow-Robin spaces).

Figure: B – MRI brain – shows Cerebral atrophy a patient with Alzheimer disease with increasing memory disturbance. Bilateral cerebral atrophy with prominent Sylvian fissures (green overlay) is seen.

1: caudate nucleus; 2: putamen; 3: thalamus

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MYASTHENIA GRAVIS

- Definition: Myasthenia gravis (MG) is an autoimmune neuromuscular disease characterized by generalised muscle weakness. The pathophysiology of MG involves autoantibodies directed against postsynaptic acetylcholine receptors (AChR), thereby impairing neuromuscular transmission.
- Myasthenia gravis is type-III hypersensitivity reaction.
- Most common neuromuscular junction (NMJ) disorder, Most common in young women with HLA-DR3 (CMDT-2024)
- Sex: Female > male (3:2)
- Peak incidence: in male is 40-70 years of age and in female 20-40 years of age

Etiology

- Auto-reactive antibodies directed against postsynaptic ACh receptors or receptor-associated proteins
- Association with other autoimmune diseases, including: Hashimoto thyroiditis, Rheumatoid arthritis, Sarcoidosis and Systemic lupus erythematosus (SLE)
- Associated conditions
 - Thymoma (the most common primary tumor in the anterior mediastinum) in 10-15% of patients
 - Thymic hyperplasia in 65% of patients
 - Graft-versus-host reaction after allogeneic stem cell transplantation (especially in children)

Classification

Main clinical forms

- Ocular myasthenia: only the extraocular and/or eyelid muscles
- Generalized myasthenia: All skeletal muscles involved., Especially ocular, bulbar, limb, & resp. muscles

Clinical features

Clinical course

- Symptoms worsen with increased muscle use throughout the day and improve with rest.
- Other factors that can exacerbate the weakness, including:
 - Medications that interfere with neuromuscular transmission: Beta blockers, Benzodiazepines, aminoglycosides, fluoroquinolones, low-potency antipsychotics, tricyclic antidepressants and quinine, procainamide, muscle relaxants & neuromuscular-blocking drugs related to anaesthesia
 - Other exacerbating factors: heat, emotional factors, stress, menstruation, pregnancy, and intercurrent infections.

- Presentation: **Fatigable weakness** of skeletal muscles in which smaller muscles responsible for fine movements (e.g., eye muscles) tend to be affected first, while larger muscles become affected later on.
 - Eye muscle weakness: most common initial symptom → **Triad of: Ptosis, Diplopia & Blurred vision**
 - Bulbar muscle weakness: patient will have slurred speech, Difficulty chewing and/or swallowing
 - Proximal limb weakness: difficulty rising from a chair, difficulty climbing stairs and Brushing hair
 - Respiratory muscle weakness: causes dyspnoea, aspiration pneumonia → Life-threatening exacerbations of myasthenia (so-called myasthenic crisis, requiring immediate ICU admission where respiratory function can be monitored and ventilator support is readily available).

Physical examination findings

- Curtain sign: Lifting the more ptotic eyelid reveals ptosis in the contralateral eyelid.
 - According to Hering's law of equal innervation, the muscles of both eyelids receive equal innervation
 - Manual lifting of the more ptotic eyelid → elimination of the central compensation required to keep the more ptotic eyelid elevated → less innervation to both eyelids → relaxing of the contralateral levator palpebrae superioris → enhancement of ptosis in contralateral eyelid
- Cogan lid twitch sign
 - The patient is asked to gaze downward for 10-20 seconds and then to look straight ahead
 - The affected upper eyelid briefly twitches
- Simpson test
 - Provocation test used to reproduce eyelid fatigue
 - Positive if looking upward for > 1 minute (without lifting the head) provokes eyelid fatigue
- Ice test: ice pack placed on one eye for 5 minutes → temporary improvement of eyelid fatigue

DIAGNOSTIC WORKUP

1. **Autoimmune antibodies test**
 - ✓ **AChR antibody test (most specific test):** 80–90% of patients with generalized myasthenia gravis have antibodies. 100% of patients with thymoma have antibodies.
 - ✓ **Antibodies to muscle-specific tyrosine kinase (Anti-MuSK):** Certain patients without antibodies to ACh receptors have serum anti-MuSK which should therefore be determined; these patients are more likely to have facial, respiratory, and proximal muscle weakness than those with antibodies to ACh receptors.
 - ✓ **Other antibodies associated with myasthenia gravis include:** LDL receptor-related protein 4 (LRP4) and agrin, but tests for these antibodies are not widely commercially available.
2. **Electromyography (EMG):** Shows demonstration of a **decrementing muscle response to repetitive 2- or 3-Hz stimulation of motor nerves** indicates a disturbance of neuromuscular transmission
3. **CT scan chest (without contrast):** every newly diagnosed myasthenia gravis patient to rule out thymoma
4. **Edrophonium test (Tensilon test)** – High false positive rate
 - ✓ Used to diagnose myasthenia gravis before AChR antibody test became the common method
 - ✓ Symptoms improve rapidly after administration of a short-acting acetylcholinesterase inhibitor

TREATMENT GUIDELINES

1. **Pharmacotherapy**
 - ✓ **First line:** cholinesterase inhibitors (Neostigmine, Pyridostigmine)
 - » Provide symptomatic benefit without influencing the course of the disease.
 - » **Drug of choice:** Pyridostigmine (Amygra, Mestinon)
 - ✓ **Supplemental immunosuppressants:** if symptoms persist despite anticholinesterase treatment
 - » **Glucocorticoids:** Prednisone or Prednisolone
 - » **Alternatives:** Azathioprine, cyclosporine, mycophenolate mofetil, rituximab, and Eculizumab
 - ✓ **Medications which may exacerbate myasthenia gravis should be avoided as mentioned above.**
2. **Surgery** → Thymectomy → Should be performed if thymoma is present
 - ✓ Can be beneficial even if a thymoma is not present (multicenter randomized trial)
 - ✓ Thymectomy should be considered in all patients younger than 65 years old.
 - ✓ Not for patients with MuSK antibody-associated myasthenia gravis without a thymoma



TREATMENT OF MYASTHENIA GRAVIS (MG)

1. **Tab. Pyridostigmine 60mg (Amygra, Mestinon)**
 - » **Dosage:** Starting at 30 mg/dose and increasing if required to 60 mg/dose orally four or five times daily with a maximum dose of 360mg/day. (Oxford textbook of medicine 6th edition)
 - » Abdominal cramping is a common side effect, relating to muscarinic overstimulation, and responds to **Tab. Propantheline**, ideally taken 30 min before each dose of pyridostigmine.
2. **OR Tab. Neostigmine 15mg at dose 7.5–30mg (average, 15 mg) x per orally four times daily**
3. **If stable patient with MG responded poorly to anticholinesterase drugs, then add on corticosteroids:**
4. **Tab. Prednisolone 5mg (Deltacortril, Rapiport)**
 - » **Dosage:** Deltacortril at 10–20mg orally daily or alternating day and increased by 10mg increments weekly to a target of 1 mg/kg/day (Maximum daily dose 100 mg).
 - » Introduction of high dose of prednisolone may exacerbate transient myasthenic weakness, even develop respiratory failure and should generally be done in hospital. (CMDT-2024, Oxford textbook)
5. **If not responded with corticosteroids the addition of azathioprine is beneficial with Prednisolone**
6. **Tab. Azathioprine 50mg (Imuran, Amarin) at dose 2.5mg/kg/day, the starting dose is 25 or 50mg daily, increased by 25 or 50 mg daily, each week (or more rapidly as an inpatient) until the target dose is reached. During therapy, weekly tests of CBC and LFTs are required.**
7. **Eculizumab in patients who have disease refractory to at least two alternate immunosuppressive therapies**
 - » **Inj. Eculizumab 300mg/30ml (Soliris) x IV at dose 900mg weekly for four doses, followed by 1200mg at week 5, and then 1200mg every 2 weeks).**
 - » **Pre-vaccination:** Patients must be vaccinated against meningococcus before receiving
8. **In patients with myasthenia crisis (major disability):** ICU admission, Resuscitation and ventilation, and Plasmapheresis or intravenous-immunoglobulins (IVIG) therapy (both have similar efficacy). See ER section.

GUILLAIN-BARRÉ SYNDROME (GBS)

- Definition: Guillain-Barré syndrome (GBS) is an acute postinfectious polyneuropathy characterized by symmetric and ascending flaccid paralysis. In affected patients, cross-reactive autoantibodies attack the host's own axonal antigens, resulting in inflammatory and demyelinating polyneuropathy.

Etiology

Overview

- » Acute or subacute progressive polyradiculoneuropathy. Also called as acute Idiopathic polyneuropathy
- » About two third (⅔) of GBS patients experience symptoms of an upper respiratory (URTI) or gastrointestinal (GIT) infection 1–4 weeks prior to onset of GBS.
- » The causal connection between pathogens and GBS is still undetermined.

Associated pathogens

- » **Campylobacter jejuni:** campylobacter enteritis is commonest associated disease with GBS.
- » **Cytomegalovirus:** most common virus associated with GBS
- » **Other:** HIV, Influenza, Zika virus, Epstein-Barr virus, SARS-CoV-2, Mycoplasma pneumoniae

- Vaccination: There have been reports of small increases in incidence after administration of certain vaccines. In the USA, Guillain-Barré syndrome is listed as vaccination injury for the seasonal influenza vaccines.

Pathophysiology

- » **Type-II HSR** → post-infectious autoimmune reaction after 1-3 weeks of URTI or GIT infection that generates cross-reactive antibodies (molecular mimicry/antigenic-mimicry)
- » Infection triggers humoral response → formation of autoantibodies against gangliosides (e.g., GM1, GD1a) or other unknown antigens of peripheral schwann cells → immune-mediated segmental demyelination → axonal degeneration of motor and sensory fibers in peripheral and cranial nerves (CN-III to CN-XII)

Diagnostics investigations

- » **Cerebrospinal fluid:** Albuminocytologic dissociation
 - » Increase Protein levels and normal white blood cell count in cerebrospinal fluid (CSF)
 - » CSF cell counts higher than 50 cells per µg CSF indicate that GBS is unlikely
- » **Serological screening**
 - » To identify potential pathogens (e.g., Campylobacter jejuni)
 - » Detection of antibodies directed against gangliosides (e.g., Anti-GM1 antibodies)
- » **Spirometry:** To ensure adequate respiratory function → Intubate early if necessary
- » **Electroneurography (Nerve conduction studies)**
 - » Decrease nerve conduction velocity (NCV) due to demyelination
 - » Reduced amplitude in compound muscle action potentials
 - » Increase F-wave latency
- » **Electromyography (EMG)**
 - » **Signs of denervation:** characteristic of axonal lesions
 - » Pathologic spontaneous activity (unfavorable prognostic sign)
- » **ECG:** autonomic cardiac dysregulation → impaired heart frequency variation
- » **MRI:** to rule out other causes of weakness, Findings in acute cases, may demonstrate enhancement and thickening of the intrathecal spinal nerve roots and cauda equina

Prognosis

- » = 70% of patients with GBS have a good prognosis
 - Disease progression peaks 2–4 weeks after the onset of symptoms.
 - Symptoms then recede in reverse order of their development; (i.e., the last symptoms to appear resolve first as Schwann cells remyelinate peripheral nerve axons).
- » In GBS 3 to 7% of patients die due to acute complications such as:
 1. Respiratory paralysis (apnea)
 2. Pulmonary infection/embolism
 3. Cardiac dysfunction
- » 6-months after onset, ~ 20% of affected individuals are still unable to walk unaided.
- » Death can occur as many as > 30 days after onset of symptoms, during the recovery phase.
- » **Note:** Although GBS is considered an autoimmune disease, glucocorticoids are not recommended for treatment. They have not shown to hasten recovery or affect the long-term outcome.

△ Guillain-Barré syndrome (GBS)

C/C:

Initial symptoms

- » Back and limb pain
- » Paresthesias affecting distal extremities

Advanced symptoms

Ascending paralysis

- » Bilateral flaccid paralysis
- » Spreads from the lower to the upper limbs in a "stocking-glove" distribution

» **Landry paralysis:** involvement of the respiratory muscles → Resp. failure

Muscle reflexes

- » Reduced or absent
- » Commonly beginning in the lower limbs

Paresthesias

- » Peripheral, symmetric
- » Usually affecting hands and feet

» **Neuropathic pain:** develops in about ⅓ of affected individuals

Autonomic dysfunction

- » CVS: Arrhythmia, blood pressure dysregulation (↑ or ↓)
- » Voiding dysfunction
- » Intestinal dysfunction

Cranial nerve involvement

- » Facial diplegia due to frequent bilateral facial nerve involvement
- » Also affects glossopharyngeal nerve (IX) and vagal nerve (X)

Subtypes and variants of GBS

1. Acute inflammatory demyelinating polyneuropathy (AIDP)
2. Chronic inflammatory demyelinating polyneuropathy (CIDP)
3. Miller-Fisher syndrome
4. Multifocal motor neuropathy (MMN)
5. Acute motor axonal neuropathy (AMAN)

NOTE: Patients should be admitted to ICUs if their forced vital capacity is declining, and intubation is considered if the forced vital capacity reaches 15 mL/kg, the maximum inspiratory pressure reaches -30mmHg, or dyspnea becomes evident. Declining oxygen saturation is a late indicator of neuro-muscular respiratory failure. Respiratory toilet and chest physical therapy help prevent atelectasis. Marked hypotension may respond to volume replacement or pressor agents.



TREATMENT OF GUILLAIN-BARRÉ SYNDROME (GBS)

1. Airway:

- » Ensure patient is maintaining own airway
- » Sit patient up, Assess and secure stable airway
- » Obtained a set of observation
- » Intubation may be indicated

2. Breathing:

- » Check SpO₂, Aim to keep saturation 94-98%
- » Give supplementary oxygen

3. Circulation:

- » Pass IV line (IV cannula)
- » Inj 0.9% N/S x IV x BD
- » **Vitals monitoring:** Check BP, PR, RR, Temp., SpO₂
- » **Send labs:** CBC, BUN, creatinine, LFTs, PT INR, RBS, & ABGs.
- » **Treatment two choices:** both equally helpful

↳ **Plasmapheresis:** is best performed within the first few days of illness and is particularly useful for clinically severe or rapidly progressive cases or those with ventilatory impairment.

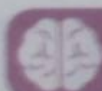
- » **In adults:** equivalent outcome as IVIG
- » **In children:** only recommended in children with rapidly progressing or severe disease

↳ **Intravenous immunoglobulins (IVIG)**

- » **Brand:** Inj. Pentaglobin, Inj. Gemunex-C, inj. HiGlobin, inj. Gammaraas,
- » **Dosage:** 400mg/kg/day for 5 days
- » **Inj. Ceftriaxone 1g** (Oxidil, Titan) x IV x BD
- » **Thromboprophylaxis is important:**
Inj. Enoxaparin sodium 40mg, 60mg or 80mg (Clexane) x SC x once daily (100 IU/kg or 1.5mg/kg)
- » **Inj. Omeprazole 40mg** (Ruling, Risek) x IV x OD
- » **Inj. Hydrocortisone 250mg** (Solu-cortif) 100-250mg x SOS

4. Disability & Exposure

- » Consider admission in ICU
- » Monitor pupillary reflexes and GCS level
- » **Monitor cardiac and respiratory function**
- » Identify and treat underlying cause
- » Prevention of decubitus ulcer and/or thrombosis/PE
- » **General support**
 1. Prevent decubitus ulcer and/or thrombosis (esp. pulmonary embolism)
 2. Changing position 1 hourly to prevent pressure ulcer
 3. Physiotherapy
 4. Chest compression



MULTIPLE SCLEROSIS (MS)

- ☛ **Definition:** Multiple sclerosis (MS) is a chronic degenerative disease of the CNS characterized by demyelination and axonal degeneration in the brain and spinal cord, which are caused by an immune-mediated inflammatory process.
- ☛ **More common in female > male (3:1), Age of onset:** 20–40 years of age

Etiology

The etiology of multiple sclerosis is unclear; it is believed to develop in genetically predisposed people who have been exposed to certain environmental factors.

- ☛ **Genetic predisposition**
 - » Presence of HLA-DRB1*15 allele increases the risk of multiple sclerosis (MS)
 - » Presence of HLA-A*02 allele appears to be protective against multiple sclerosis (MS)
 - » 35% disease concordance among monozygotic twins
 - » 3–4% disease concordance among first-degree relatives
- ☛ **Environmental risk factors**
 - » Low vitamin-D levels (insufficient intake, decreased exposure to UV radiation)
 - » Cigarette smoking
 - » **Pathogens:** EBV, HHV 6
 - » Obesity early in life

Clinical course of Multiple sclerosis (MS)

Main clinical patterns/phenotypes are:

1. **Relapsing-remitting MS (RR-MS) – (85–90%):** Most common clinical course, discrete attack and complete recovery.
2. **Secondary progressive MS (SP-MS):** Begin as Relapsing-remitting MS (RR-MS) characterized by continuous worsening of neurological function that occurs independently of exacerbation events.
3. **Primary progressive MS (PP-MS) – (10–15%):** Symptoms continuously worsen from the onset of the disease.
4. **Progressive relapsing MS (PRMS) – (<5%):** least common form, progressive worsening of condition from the beginning.
5. **Malignant MS/Aggressive MS:** refers to disease with a rapid progressive course, leading to significant disability in multiple neurologic systems in a relatively short time after disease onset.
6. **Tumefactive MS:** it is an acute tumor-like MS variant in which some patients with demyelinating disease present with large (>2 cm) acute lesions, often associated with edema or ring enhancement.

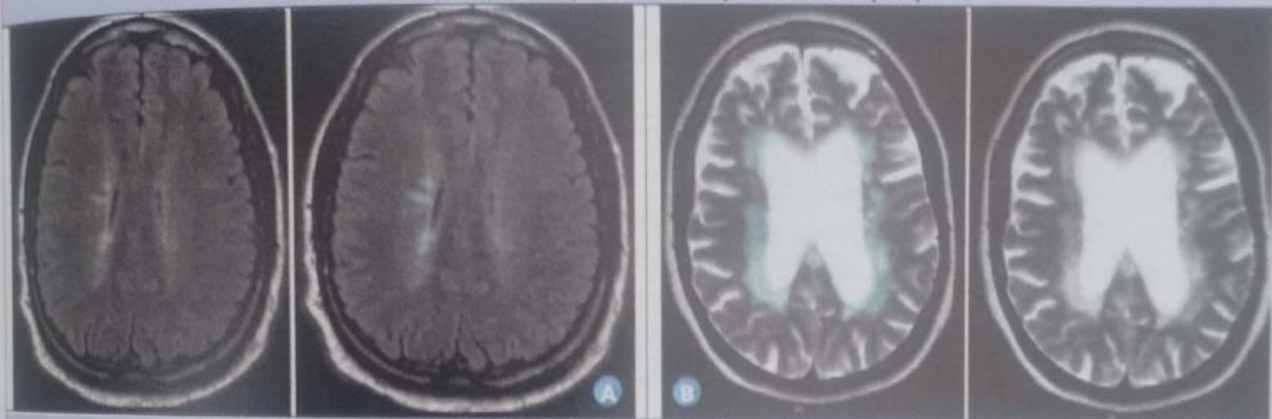
Clinical features of Multiple sclerosis (MS)

- ☛ No single group of signs or symptoms is diagnostic of Multiple sclerosis (MS)
- ☛ **Onset:** May be abrupt/insidious, vary from trivial to severe form.
- ☛ Presentation varies and depends on the anatomical site of lesions and severity.
- ☛ It has been called as the modern 'great imitator'.
- ☛ Multiple sclerosis (MS) commonly involve pyramidal tract, optic nerve, posterior cord, cerebellum and MLF.
- ☛ **Constitutional symptoms:** Fatigue, headache
- ☛ **Optic nerve involvement → Optic neuritis:** Most often the earliest manifestation, typically unilateral, can be painful, Impaired vision and color blindness and Relative afferent pupillary defect (Marcus Gunn pupil)
- ☛ **Lesion in the medial longitudinal fasciculus (MLF) → Internuclear ophthalmoplegia (INO):** Inability to adduct the eye on lateral gaze with a demyelinating lesion affecting the ipsilateral medial longitudinal fasciculus.
- ☛ **Demyelination of spinal cord tracts**
 - » **Lhermitte sign:** a shooting electric sensation that travels down the spine upon flexion of the neck
 - » **Pyramidal tract lesion:** UMN weakness, spasticity, hyperreflexia, +ve Babinski sign, impaired gait
 - » **Dorsal spinal column lesion:** loss of vibration and fine-touch sensation, numbness, paresthesias, sensory ataxia usually involving the trunk or one or more limbs
 - » **Neuropathic pain and Absent abdominal reflex**
- ☛ **Cerebellar involvement:** poor postural control, imbalance, gait dysfunction, Charcot neurological triad of scanning speech, nystagmus, and intention tremors
- ☛ **Cranial nerve palsies:** diplopia, trigeminal sensory neuralgia, facial palsy
- ☛ **Autonomic dysfunction:** bowel and bladder neurogenic disorders (urinary incontinence), impaired sexual function
- ☛ **Changes in mental state:** depression, emotional changes, memory deficits, impaired concentration
- ☛ **Uhthoff phenomenon:** a reversible exacerbation of neurological symptoms following an increase in body temperature, e.g., physical exertion, a warm bath, or fever

General principles and diagnostic approach to Multiple sclerosis (MS)

- Diagnosis of Multiple sclerosis (MS) depends on a combination of clinical findings (e.g., optic neuritis, Lhermitte sign, sensory abnormalities, and cerebellar signs), radiological imaging, and laboratory test results.
- Consider early specialist consultation (Neurologist) for patients with history and clinical features suggestive of MS.
- The McDonald Criteria for both dissemination in time (DIT) & dissemination in space (DIS) must both be met to confirm a diagnosis of Multiple sclerosis (MS)
 - DIT: the appearance of new CNS (neurological lesions) over time that can be confirmed clinically, with radiological imaging, or with CSF analysis
 - DIS: the presence of lesions in different regions of the CNS that can be confirmed clinically or in MRI
 - In some cases, electrophysiological, CSF analysis, and laboratory test may be necessary to support the diagnosis and exclude differential diagnoses.
- MRI is the investigation of choice for the diagnosis and monitoring of Multiple sclerosis (MS)
 - Characteristic abnormalities are found in >95% of patients
 - MRI brain (with and without gadolinium):** all patients with suspected MS
 - MRI spinal cord (with and without gadolinium):** to increase diagnostic yield (e.g., in patients with non-diagnostic brain MRI or symptoms of partial myelitis)
 - Typical findings on MRI: Multiple sclerotic plaques** (most commonly found in the periventricular white matter) with finger-like radial extensions (**Dawson fingers**) related to demyelination and reactive gliosis.

MRI brain and cervical spine of Multiple sclerosis (MS)



MRI brain (T2-weighted; axial plane) shows Periventricular demyelinating lesions

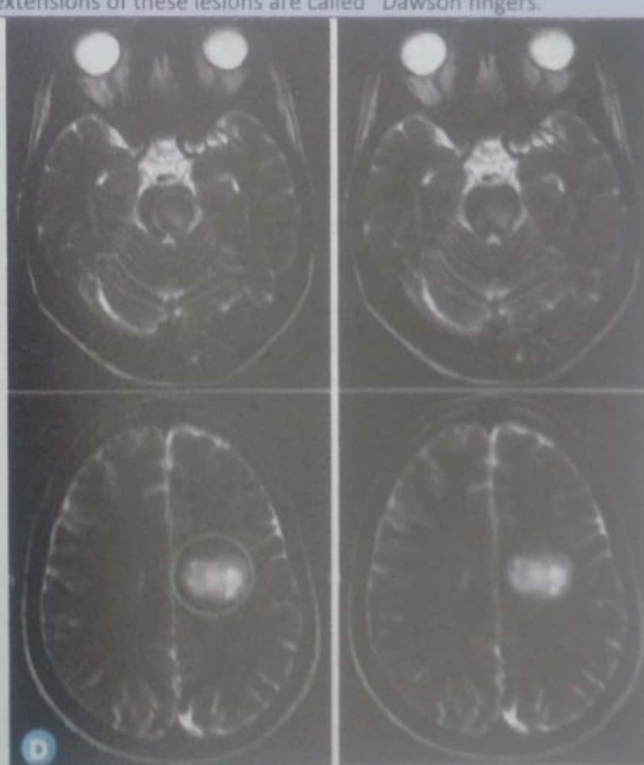
Figure: A – Periventricular areas of hyperintensity which stretch out perpendicular along medullary veins (Dawson's fingers; green overlay). Figure: B – There are extensive demyelinating lesions (plaques) bilaterally, appearing as hyperintensities in the periventricular white matter (green overlay). The finger-like radial extensions of these lesions are called "Dawson fingers."



MRI cervical spine (T2-weighted sagittal, paramedian level)

Figure: C – Evidence of a hyper-intensity of the spinal cord at the level of C4. (For orientation reasons: C2, indicated as 2 in the image, can be well-recognized at the dens of the axis)

Figure: D – Multiple sclerotic plaques in the subcortical white matter → Solitary hyperintense demyelinated plaques in the telencephalon; multiple periventricular and mesencephalic hyperintensities. **Diagnosis: Multiple sclerosis**



MRI brain (T2-weighted; axial view)



Additional diagnostic investigations: Consider further testing for patients with non-diagnostic MRI and to rule out differential diagnoses.

1. **CSF examination:** commonly performed to support MS diagnosis and rule out other conditions
 - » Increased IgG, total CSF protein, CSF IgG index.
 - » **Protein electrophoresis:** Oligoclonal IgG bands detected by agarose gel, but Oligoclonal bands in the CSF but not in blood support diagnosis of MS.
 - » **Moderate lymphocytic pleocytosis,** increased myelin basic protein
2. **Evoked potentials:** Consider visual evoked potentials for patients with symptoms related to vision.
 - » Can provide objective evidence of lesions
 - » May show evidence of increased latency, which occurs due to slowed optic nerve conduction.
3. **Laboratory tests:** to rule out other diagnoses, based on clinical suspicion
 - » **Test commonly ordered:**
 - Complete blood count (CBC), serum vitamin B12, serum TSH, serum ESR
 - Anti-nuclear antibody (ANA), rapid plasma reagin (RPR), serologic testing for Lyme disease
 - **Others:** specific autoantibodies (e.g., antiphospholipid antibodies, anti-SSA, anti-SSB), HIV testing.

McDonald criteria for Multiple sclerosis (MS)

Attack	Lesion	Additional criteria for diagnosis MS
2 or more	2 or more	» Non-clinical evidence alone will suffice
2 or more	1 lesion	» Dissemination in space (DIS) of MR (or await further clinical attack implicating a different CNS site)
1 attack	2 lesion	» Dissemination in time (DIT) on MR (or await further clinical attack implicating a different CNS site)
1 attack	1 lesion	» DIS and DIT (or await further clinical attack implicating a different CNS site)
0 attack		» One year of disease progression (Retrospective or prospective) and at least 2 out of 3 criteria ▪ Dissemination in space (DIS) in the brain ▪ Dissemination in space (DIS) in the spinal cord based on 2 or more T2 lesions ▪ Positive CSF
Progression from onset		



TREATMENT OF MULTIPLE SCLEROSIS (MS)

General principles

- **All patients:** Refer to a neurologist for specialized management.
- **Acute exacerbations:** Treat all acute exacerbations that affect physical functioning.
 - » **First line:** high-dose IV or PO corticosteroids (methylprednisolone)
 - » **Alternatives:** Plasmapheresis or Adrenocorticotrophic hormone (ACTH) gel (ACTHAR Gel 80IU/ml)
- **Long-term management:** Combine pharmacological and non-pharmacological measures to prevent exacerbations and improve quality of life.
 - » Disease-modifying MS therapy
 - » **Lifestyle modifications:**
 - Exercise, smoking cessation
 - Management of comorbidities (e.g., cardiovascular disease, sleep disorders)
 - Vitamin-D³ supplementation (Cholecalciferol) may be beneficial
 - » Management of symptoms (e.g., spasticity, pain, bowel and bladder dysfunction)

Management of acute exacerbations

If an acute exacerbation of MS is suspected, a specialist should be consulted immediately for management.

Preferred therapy:

- **High-dose corticosteroids pulse therapy:** Inj. Methylprednisolone 1000mg (Solu-Medrol) at dose 1000 mg IV x once daily for 3 to 5 days, Followed by oral prednisolone 5mg (Deltacortril) at 60-80mg daily for 1 week with a taper over the ensuing 2-3 weeks
- Start measures to prevent complications of corticosteroids therapy
 - Consider PPIs: Omeprazole 40mg (Risek) or Esomeprazole 40mg (Nexum) x orally or IV x OD
 - Monitoring for hyperglycemia: monitoring blood sugar level (BSR/RBS)
- Alternatives: Plasmapheresis exchange of blood plasma, ACTH gel

➤ Additional considerations

- Perform a thorough neurological examination and compare with the patient's baseline.
- Evaluate for possible infectious triggers.
- Consider hospital admission for patients with disabling symptoms (e.g., loss of vision, difficulty with ambulation, dysphagia).
- Supportive care: physical therapy, occupational therapy, and/or speech and swallow evaluations

➤ Disease-modifying MS therapy

- There are multiple disease-modifying drugs available to treat MS.
- The decision about agent requires careful consideration of: Individual patient's characteristics (e.g., clinical phenotype, comorbidities) and Medication side effects.
- All patients receiving disease-modifying therapy for MS should use birth control.

COMMONLY USED DISEASE-MODIFYING MS DRUGS BY CLINICAL PHENOTYPE

1. Clinically isolated syndrome

- Inj. Interferon beta (IFN- β) therapy
 - Interferon β -1a (Rebif 44mcg/0.5ml) x 44mcg x TDS/week
 - Interferon β -1a (Avonex 30mcg/0.5ml) x 30mcg x IM once/week
 - Interferon beta-1b (Betaseron 0.3mg/vial, Extavia 0.3mg/vial) x at dose 0.25mg x SC on alternate days
- Inj. Glatiramer acetate 20mg/ml or 40mg/ml (Copaxone, Mylan, Glatopa) at dose 20mg subcutaneously (SC) x OD or 40mg SC x TDS x weekly
- Tab. Teriflunomide 14mg (Aubagio) x 14 mg or 7 mg orally daily

2. Relapsing-remitting MS (RRMS)

- Interferon beta (IFN- β) therapy
- Pegylated interferon β -1a (Plegridy) x 125mg x SC x once every 2 weeks
- Glatiramer acetate: 20mg SC x OD or 40mg SC x TDS x weekly (as above)
- Dimethyl fumarate: 240mg per orally x BD
- Tab. Teriflunomide 14mg (Aubagio) x 14 mg or 7 mg orally daily
- Sphingosine 1-phosphate receptor modulators:
 - Cap. Fingolimod (Gilenya 0.5mg) x 0.5mg orally daily
 - Tab. Siponimod (Mayzent 0.25mg or 2mg) x 0.25mg orally daily, titrated over 5 or 6 days to 1 or 2mg orally daily, depending on CYP2C9 genotype
 - Tab. Ponesimod (Ponvory 20mg) x Titrate from 2mg orally daily to 5mg in 1-mg increments every 2 days, then by 1mg daily to 10mg by day 12, and then to 20mg daily on day 15
 - Cap. Ozanimod (Zeposia 0.92mg) x 0.23mg orally daily on days 1-4, 0.46mg daily on days 5-7, and 0.92mg daily thereafter
- Monoclonal antibodies:
 - Inj. Natalizumab (Tysabri 300mg/15ml) x 300mg intravenously (IV) monthly
 - Inj. Ocrelizumab (Ocrevus 300mg/10ml) x 300mg intravenously (IV) on day 1 and day 15, followed by 600mg every 6 months.
 - Inj. Alemtuzumab (Lemtrada 12mg/1.2ml) x 12mg IV daily for 5 days; 3-day course given 1 year later
 - Inj. Ofatumumab (Kesimpta 20mg/0.4ml) x 20mg x SC weeks 0, 1, 2, 4, and monthly thereafter
 - Inj. Mitoxantrone (25mg/12.5ml, 20mg/10ml, or 30mg/15ml) x 12mg/m² intravenously every 3 months; maximum lifetime dose, 140mg/m²
 - Tab. Cladribine (Mavenclad 10mg) at dose 1.75 mg/kg per orally divided between weeks 1 & 5, repeated once in 1 year.

3. Secondary progressive MS (SPMS)

- All disease-modifying therapies may be used for active SP-MS.

4. Primary progressive MS (PPMS)

- Inj. Ocrelizumab (Ocrevus 300mg/10ml) x 300mg intravenously (IV) on day 1 and day 15, followed by 600mg every 6 months.



SUPPORTIVE CARE & SYMPTOMATIC MANAGEMENT OF MULTIPLE SCLEROSIS (MS)

Rx

Consider any of the following measures in a management plan tailored to the individual patient:

☞ **General measures**

- » Encourage physical activity.
- » Close follow-up with neurology and primary care
- » Ancillary referral as needed (e.g., physical therapists, occupational therapists, psychologists)
- » Screen for major depression and start therapy with antidepressants as needed (See psychiatry section)
 - Tab. Escitalopram 10mg (Estar, Cipralex, Citanew) x once daily after breakfast
 - OR Tab. Fluoxetine 20mg (Prozac, Flux, Depex) x once daily after breakfast increase dose according patient response up to 40-60 mg in twice daily divided doses
 - OR Tab. Sertraline 50mg or 100mg (Zoloft, Sert, Freedep) x 50mg to 100mg after breakfast

☞ **Urinary dysfunction** (see dosages and protocol in urology section)

- » **Urinary frequency**
 - Pelvic floor physical therapy
 - Bladder training
 - Consider medications: Anticholinergics (Oxybutynin) and antimuscarinics (Tolterodine).
- » **Urinary retention:**
 - Consider intermittent catheterization
 - Medications: Parasympathomimetic drugs – (Bethanechol)

☞ **Bowel dysfunction** (see protocol of constipation in GIT section)

- » **Dietary fiber:** Isphagol husk, Fibo, Fibrocol
- » **Increase fluid/water intake**
- » **Consider laxatives:** Senna extract (Ezilax, senokot), Lactulose (Lilac, Duphalac), Sodium picosulphate (Laxoberon tab/syp., skilax tab./drops) & stool softeners as needed: Docusate sodium (Cap. Colac 50mg)

☞ **Spasticity**

- » Stretching, avoidance of triggers (e.g., certain positions, pain, constipation)
- » **Medications:** Tab. Baclofen 10mg or 20mg (Baclast, Lioresal, Baclin), Tab. Tizanidine 2mg, or 4mg or 6mg (Ternalin, Movax, Musidin), Cap. Dantrolene sodium 25mg (Danlene, Relaxo) and Botulinum toxin.

☞ **Tremors:** Tab. Propranolol 10mg, or 40mg (Inderol, Cardinol)

☞ **Neuropathic pain** (See doses in antipressants and anti-convulsants section)

- » **Tricyclic antidepressants:** Tab. Amitriptyline 25mg (Tryptanol, Amyline)
- » **SNRIs:** Cap. Duloxetine 20mg or 30mg (Cymbalta, Lyta, Dulan)
- » **Anticonvulsants:** Tab. Carbamazepine 200mg, 400mg (Seizunil, Tegrol), Cap. Gabapentin 300mg or 400mg (Neogab, Gabix), Cap. Pregabalin 50mg, 75mg, 100mg or 150mg (Gabica, Syngab, Prelin, Lyrica)
- » **Transcutaneous electrical nerve stimulation**

☞ **Walking difficulties:**

- » Mobility aids – canes, walkers

» **Medication:** consider Tab. Dalfampridine 10mg (Ampyra, Fampyra) x twice daily

☞ **Fatigue:** Consider medications such as Tab. Modafinil 200mg (Dowvigil, V-zac) x per orally x every morning

☞ **Sexual dysfunction** (see prescription on erectile dysfunction)

- » **Consider medications for erectile dysfunction:** Tab. Sildenafil 50mg, 100mg (Viagra)
- » Nonpharmacological measures (e.g., vaginal lubricants, intracavernous injection therapy) as needed.

☞ **Psychotherapy:** to reduce potential psychological issues (e.g., depression)

SEIZURES & EPILEPSY (SEIZURE DISORDERS)

Definition

- Seizure (Fits/Convulsions): an excessive abnormal clinical activity of cortical neurons (synchronized and high-frequency neuronal depolarization) that results from abnormal electrical discharge in the brain which results in transient neurological symptoms
- Epilepsy: a chronic neurologic disorder characterized by recurrent tendency to have seizures at least two or more seizures in two different time and space in 24 hours
- Status epilepticus is continuous or recurring seizure(s) that may result in brain injury; defined as > 5 min.

Types of epilepsy - underlying pathogenesis

- Idiopathic (primary): When there is no any underlying cause, presumed to be genetic
- Symptomatic (secondary):
 - Due to structural changes in the brain: Vascular (Stroke, SAH, ICH, AV Malformation), Infective cause (Meningitis, lupus cerebritis, Encephalitis, toxoplasmosis, neurocysticercosis, cerebral abscess), Head trauma (EDH, SDH), Tumors (Primary & secondary), Metabolic (Hypoglycemia, hyponatremia, hypocalcemia, hypomagnesemia, uremia, hepatic encephalopathy, hyperthermia, organ failure, sarcoidosis), Medications (Tramadol, clozapine, cyclosporine, fluoroquinolones, penicillin, TCAs, lithium, ciclosporin, Isoniazid, metronidazole, chloroquine, illicit drugs, amphetamine, toxins (OP poisoning), cocaine, Drug withdrawal (Benzodiazepine, barbiturates, alcohol, delirium tremens, heroin/cannabis)
 - Described by location (Focal seizures) of the lesion: Temporal lobe epilepsy (most common), frontal lobe epilepsy, parietal lobe epilepsy and occipital lobe epilepsy.

Classification of seizures

- Partial (Focal) seizures: when seizures activity is confined to one part of cerebral cortex (seizures originates within the networks of a single cerebral hemisphere of the brain)
- Generalized seizures: when seizures activity involving whole brain (seizures originates from both cerebral hemispheres of the brain)
- Febrile Seizures: seizures or convulsions that occur in young children and are triggered by fever.

Sub-types of seizures

1. Partial (Focal) seizures

- Simple partial seizures: focal onset seizures without ASOC (consciousness is spared)
- Complex partial seizures: focal onset seizures with ASOC (consciousness is impaired)

2. Generalized seizures

- Myoclonic seizures: » Patients can present with sudden & repetitive jerking (muscle twitching) of limbs
» Infantile spasms are a subtype type of myoclonic epilepsy that typically begins between the ages of 3 and 12 months of age and may persist for several years.

- Myoclonic-atonic: » Myoclonus followed by a brief loss of tone

- Myoclonic-tonic: » Myoclonus followed by a brief increase in tone

- Tonic-clonic seizures: » Also known as **grand-mal seizures**. Most common type, usually lasts 1-3 minutes
» Prodromal symptoms may occur up to hours before seizure onset (e.g., sleep disturbances, lightheadedness, mood changes, anxiety/irritability, impaired concentration)

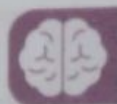
- » Loss of consciousness (sudden and without warning)

- » Bladder or bowel incontinence

- » Tongue-biting, tongue lacerations

- » Motor symptoms

- Tonic phase



	- Generalized muscle contractions: rotated eyes, apnea, lateral tongue biting, pooled oral secretions, cyanosis, & characteristic loud moan (ictal cry) ↑ sympathetic tone: dilated, unresponsive pupils, ↑ heart rate, ↑ BP - Clonic phase: rhythmic muscle twitching - Postictal (after seizure) phase: Unresponsiveness, Confusion, Amnesia of the event, Aphasia, Fatigue, Muscular flaccidity and muscle pain, Headache, Hypersalivation with or without airway obstruction
☞ Tonic seizures	- Often occurs when the patient is drowsy, asleep, or after waking - Loss of consciousness - Muscle stiffening (extension or flexion of the head, trunk, and/or extremities) → Contraction can be bilateral or unilateral - Can be accompanied by autonomic symptoms (e.g., tachycardia, flushing) - Can be followed by atypical absence seizure
☞ Clonic	- Loss of consciousness - Bilateral rhythmic jerking (of the entire body or only a part)
☞ Atonic	- Atonic seizure also known as "drop seizure" or "drop attack" - Sudden loss of muscle tone. If the hypotonia is generalized, falls occur, often with substantial injury. Sudden head drop or collapse (lasts < 15 seconds). The attacks begin in infancy or childhood. Frequently mistaken for syncope or fainting
☞ Absence seizures	- Generalized nonmotor seizure, also called petit mal seizures. - Most commonly occurs in children Characteristic EEG finding: Generalized 3-4-Hz spike and wave discharges Two types: Typical absence seizures and atypical absence seizures 1. Typical Absence seizures Sudden onset and stop, Parents may report the child suddenly stop activity, Rolls eye upwards, blank stare. Patients fail to respond (unresponsiveness) - Can occur several hundred times a day and usually lasts < 10 seconds Subtle automatisms (often go unnoticed): lip-smacking, eye fluttering, or head nodding are common. Triggers: hyperventilation, flashing lights 2. Atypical absence seizures Gradual onset and stop, Parents may report the child suddenly stop activity, Rolls eye upwards, blank stare. Patients may be responsive Automatisms: lip-smacking, eye fluttering, chewing - Small hand movements (e.g., rubbing of the fingers) - Longer than typical form (10–30 seconds)

Approach to diagnosis of seizure/epilepsy

First seizure attack

- ☞ **Confirmation of seizure:** Determine if the patient had a true seizure
- ☞ If possible, identify the underlying cause at the initial presentation.
- ☞ Clinically evaluate the type of seizure (as mentioned above) and identify potential seizure triggers.
- ☞ Obtain laboratory tests to identify metabolic abnormalities.
- ☞ **Consider brain radiological imaging to evaluate for structural causes:** MRI > CT scan
- ☞ Obtain an EEG.

Previously diagnosed epilepsy

- ☞ Assess for common causes of breakthrough seizures and increased seizure frequency:
For example,
 - » Poor adherence and other medication-related issues
 - » Intercurrent infection or systemic diseases
 - » Alcohol consumption and/or recreational drug use
- ☞ Check antiepileptic drug levels.
- ☞ **Consider further investigations based on clinical suspicion:** workup for sepsis/infections, selective brain imaging.
- ☞ Consider EEG for patients with treatment-refractory seizures, those who have had a change in seizure type, or if there is insufficient information for seizure classification.

Confirmation of seizure

- » History taking
 - » History of present illness: Description of the event by the patient (aware seizure) and/or witnesses (seizure with impaired awareness)
 - Potential triggers (e.g., sleep deprivation, excessive alcohol intake)
 - Prodromal symptoms (e.g., aura)
 - During seizures and after seizures symptoms (Ictal symptoms and Postictal symptoms)
 - » Past medical history
 - History of epilepsy (including current antiepileptic drugs and adherence)
 - History of other potential underlying conditions (e.g., head trauma, stroke, tumor, CNS infection)
- » Physical examination: Attention should be paid to visual inspection (e.g., for bruises from falls, tongue bites, phakomatosis-specific skin manifestations) and evaluation for cardiovascular disorders
- » Electroencephalography (EEG): consider in patients who present with first seizure, with insufficient information for seizure classification, and/or treatment-refractory seizures. EEG is normal in 40% of epileptic patients.

Evaluation for underlying conditions

- » ECG: Rule out cardiogenic causes (e.g., cardiac arrhythmias resulting in cerebral hypoxia) in all patients with loss of consciousness during a seizure.
- » MRI: Investigation of choice for investigating potential underlying structural abnormalities.
 - » All patients with first-time focal seizures
 - » Exception: children with history & exam suggestive of benign seizure or characteristic epilepsy syndrome
- » CT scan: Less sensitive for identifying soft-tissue lesions, can be used to rule out traumatic head injuries
- » Angiography: if vascular cause (e.g., cerebral arteriovenous (AV) malformation) is suspected
- » Laboratory screening test: to identify metabolic disorders and infectious diseases, if suspected
- » Blood test:
 - » Initial routine test: CBC, blood Glucose (RBS), serum calcium, serum electrolytes, RFTs, LFTs
 - » Other consider according patient history: serum prolactin, Screening for toxicology, serum ESR, Rapid plasma reagin (RPR), serum creatine kinase, Antiepileptic drug levels (phenytoin, carbamazepine, phenobarbital)
- » Urinalysis (Urine D/R)
- » Bacterial cultures: Blood culture, urine culture, Pus culture, CSF culture)
- » CSF studies: CSF analysis, PCR, Culture
- » Endocrine studies: Thyroid function (Serum TSH, T3), Adrenal function tests and Pituitary function tests

Management guideline of epilepsy/seizures

- » The following focuses on the chronic treatment of epilepsy/seizures.
- » The treatment of acute seizures and status epilepticus are discussed in emergency section
- » Neonatal seizures and febrile seizures are discussed in paediatric section
- » Antiepileptic drugs raise the seizure threshold that is pathologically lowered in individuals with epilepsy, thereby reducing the risk of future seizures.
- » Criteria for the choice of antiepileptic drugs: Seizure type, Patient age, Comorbidities & contraindications
- » Consider vitamin-D and calcium supplementation with long-term sodium valproate → ↓ Vit-D → osteoporosis

Guidelines for choice of antiepileptic drug (AED)

Seizure type		First line drug	Second line drugs	
Partial (Focal) seizures		» Carbamazepine	» Levetiracetam	» Brivaracetam
		» Lamotrigine	» Sodium valproate	» Oxcarbazepine
		» Phenobarbital (children)	» Topiramate	» Gabapentin
Generalized seizures	Tonic-clonic (GTCS)	» Sodium Valproate	» Zonisamide	» Phenytoin
		» Levetiracetam	» Lamotrigine	» Carbamazepine
		» Phenobarbital (children)	» Topiramate	» Clonazepam
	Typical absence	» Ethosuximide	» Sodium valproate	» Clonazepam
			» Lamotrigine	
	Atypical absence	» Sodium valproate	» Lamotrigine	» Clonazepam
	Myoclonic	» Levetiracetam	» Topiramate	» Felbamate
Atonic				



Common generalised epilepsy syndromes

Syndrome	Age of onset	Type of seizure	Treatment
Childhood absence epilepsy	4 – 8 years	Frequent brief absences	Ethosuximide, valproate and Levetiracetam
Juvenile absence epilepsy	10 – 15 years	Less frequent absences than childhood absence	
Juvenile myoclonic epilepsy	15 – 20 years	GTCS, absences, morning myoclonus	Sodium valproate Levetiracetam
GTCS on awakening	10 – 25 years	GTCS, sometimes myoclonus	
Febrile seizure	6m – 5 years	simple or complex seizures	Diazepam, Lorazepam Vigabatrin
Infantile spasm (West synd.)	3 – 12 months	Generalize, subtype type of myoclonic seizure	

Guidelines for antiepileptic medication therapy

Treatment regimen and principle

- Start anti-epileptic drug after 2nd attack of seizure/fits, after the confirmation or diagnosis of epilepsy type.
- Start treatment with single first line anti-epileptic drug.
- Lowest possible dose should be given with follow-up every 2 – 3 weeks, titrate the drug dose up slowly (start low, go-slow principle). Increase the dose according to response if needed.
- If seizures control with single first line drug with specific dose → continues same dose for 2 years.
- If first drug fails (seizures continue or side-effects develop), start second 1st line drug, followed, if possible, by gradual withdrawal (taper off) of first drug slowly.
- Around 2/3 of epilepsy patients become seizure-free with monotherapy (single drug therapy)
- Combination therapy should only be given if treatment with single drug fails. In this case, drugs from different classes and/or with different pharmacologic modes of action should be tried.
- If this combination fails, check adherence and reconsider diagnosis. (Are events seizures? Occult lesion? Treatment adherence/alcohol/drugs confounding response?)
- Monitoring with routine test should be done at 1, 3 and 6 month:** CBC, LFTs, Urea & creatinine, electrolytes

Discontinuance of medication

- Treatment withdrawal may be considered if the patient has <2 seizures/year, an inconspicuous provocation EEG, normal psychological findings, and no hereditary predisposition
- Generally, medication is continued until a minimum of 3–5-year period free of seizures has been established with normal EEG results and Medications should be tapered with caution. Patients should be advised of the risks of recurrence, to allow them to decide whether or not they wish to withdraw. If undertaken, withdrawal should be done slowly, reducing the drug dose gradually over weeks or months.

Characteristics of commonly used antiepileptic drugs in adults

Generic name	Brand name	Strength available	Initial dose	Usual adult daily therapeutic dose
Tab. Sodium valproate	Epival, Dapakan, Revalp	250mg, 500mg	250mg x BD	1500 – 2000mg
Tab. Levetiracetam	Keppra, Lerace, Lumark	250mg, 500mg, 750mg	250mg x BD	1000 – 3000mg
Tab. Carbamazepine	Tegrol, Terol, Seizunil	200mg, 400mg	200mg x BD	400 – 1600mg
Tab. Oxcarbazepine	Trioptal, Telax, Oxalepsy	150mg, 300mg, 600mg	150mg x BD	900 – 1800mg
Tab. Lamotrigine	Lamictol, Lomogin, Lojin	25mg, 50mg, 100mg	25mg x BD	100 – 500mg
Tab. Topiramate	Hitop, Topagen, Torate	25mg, 50mg, 100mg	25mg x BD	200 – 400mg
Tab. Felbamate	Felbamate (Not available)	400mg, 600mg	400mg x TDS	1200 – 3600mg
Tab. Brivaracetam	Brivatam, Brivace, Brivera	50mg, 100mg	50mg x BD	50 – 100mg
Tab. Phenobarbitone	Phenobarbitone	30mg	30mg x BD/TDS	60 – 180mg
Tab. Clonazepam	Revotril, Magura, Naze	0.5mg, 2mg	0.04 – 0.2mg/kg	2 – 8mg
Tab. Vigabatrin	Sabril	500mg	500mg x BD	3000mg
Tab. Phenytoin	Dilantin, Epilantin	100mg	100mg at night	200 – 400mg
Cap. Ethosuximide	Ethosuximide	250mg	250mg x BD	500 – 1500mg
Cap. Clorazepate	Tranxene	5mg, 10mg, 15mg	5mg x BD	22.5 – 90mg
Cap. Gabapentin	Neogab, Gabix	300mg, 400mg	300mg x TDS	900 – 3600mg
Cap. Pregabalin	Gabica, Syngab, Prelin	50, 75, 100 & 150mg	50 – 75mg x BD	100 – 300mg
Tab. Zonisamide	Zonas, Zonegran	100mg	100mg x BD	200 – 600mg
Tab. Lacosamide	Lacolep, Lalap, Lacolit	50, 100, 150 & 200mg	50mg x BD	100 – 400mg

LONG TERM TREATMENT PRESCRIPTION OF EPILEPSY/SEIZURES

TREATMENT OF PARTIAL (FOCAL) SEIZURES

First line medication

- Tab. Carbamazepine 200mg (Tegrol, Terol, Seizunil)

Dosage: Initial dose 200mg x twice daily, if the target goal is not achieved, titrate up the dose by 200mg every 2 weeks. **Usual daily therapeutic dose:** 400 – 1600mg.

- OR Tab. Lamotrigine 25mg, 50mg or 100mg (Lamictol, Lomogin, Lojin)

Dosage: Initial dose 25mg x twice daily, if the target not achieved, titrate up the dose by 25mg every 2 weeks. **Usual daily therapeutic dose:** 100 – 500mg.

Second line medication

- OR Tab. Levetiracetam 250mg, 500mg, or 750mg (Keppra, Lerace, Lumark)

Dosage: Initial dose 250mg x twice daily, if the target goal is not achieved, titrate up the dose by 250mg every 2 weeks. **Usual daily therapeutic dose:** 500 – 3000mg.

- OR Tab. Oxcarbazepine 150mg, 300mg or 600mg (Trioptal, Telax, Oxalepsy)

Dosage: Initial dose 150mg x twice daily, if the target goal is not achieved, titrate up the dose by 150mg every 2 weeks. **Usual daily therapeutic dose:** 600 – 2400mg.

- OR Tab. Sodium valproate 250mg or 500mg (Epival, Dapakan, Revalp)

Dosage: Initial dose 250mg x twice daily, if the target goal is not achieved, titrate up the dose by 250mg every 3 – 7 days. **Usual daily therapeutic dose:** 750 – 2000mg.

- OR Tab. Brivaracetam 50mg or 100mg (Brivatam, Brivace, Brivera)

Dosage: Initial dose 50mg x twice daily is therapeutic, it does not require up-titration.
Maximum dose: 100mg x twice daily.

- OR Tab. Topiramate 25mg, 50mg, or 100mg (Topamax, Hitop, Topagen, Torate)

Dosage: Initial dose 25mg x nocte (at night), if the target goal is not achieved, titrate up the dose by 25mg every 2 weekly x twice daily. **Usual daily therapeutic dose:** 100 – 500mg.



TREATMENT OF GENERALIZED TONIC-CLONIC (GTCS)

First line medication

- Tab. Sodium valproate 250mg or 500mg (Epival, Dapakan, Revalp)

Dosage: Initial dose 250mg x twice daily, if the target goal is not achieved, titrate up the dose by 250mg every 3 – 7 days. **Usual daily therapeutic dose:** 750 – 2000mg.

- OR Tab. Levetiracetam 250mg, 500mg, or 750mg (Keppra, Lerace, Lumark)

Dosage: Initial dose 250mg x twice daily, if the target goal is not achieved, titrate up the dose by 250mg every 2 weeks. **Usual daily therapeutic dose:** 500 – 3000mg.

Second line medication

- OR Tab. Lamotrigine 25mg, 50mg or 100mg (Lamictol, Lomogin, Lojin)

Dosage: Initial dose 25mg x twice daily, if the target not achieved, titrate up the dose by 25mg every 2 weeks. **Usual daily therapeutic dose:** 100 – 500mg.

- OR Tab. Topiramate 25mg, 50mg, or 100mg (Topamax, Hitop, Topagen, Torate)

Dosage: Initial dose 25mg x nocte (at night), if the target goal is not achieved, titrate up the dose by 25mg every 2 weekly x twice daily. **Usual daily therapeutic dose:** 100 – 500mg. (Oxford Textbook of medicine 6th edition)

- OR Tab. Zonisamide 100mg (Zonas, Zonegran)

Dosage: Initial dose 25mg x nocte (at night), if the target goal is not achieved, titrate up the dose by 25mg every 2 weekly x twice daily. **Usual daily therapeutic dose:** 100 – 500mg. (Oxford Textbook of medicine 6th edition)





INSOMNIA DISORDER

Diagnosis of Insomnia Disorder

Clinical Evaluation:

- » **Patient History:** Gather detailed history including sleep patterns, daily routines, and any psychological or medical issues.
- » **Sleep Diary:** A sleep diary for 1-2 weeks to record sleep and wake times, naps, and sleep quality.
- » **Questionnaires:** Use standardized questionnaires such as the Insomnia Severity Index (ISI) to assess the severity and impact of insomnia.
- » **Physical examination and laboratory tests:** Rule out medical conditions that may cause or exacerbate insomnia (e.g., thyroid disorders).

Diagnostic criteria – DSM5

- » **Difficulty Initiating or Maintaining Sleep:** At least 3 nights per week (Problems initiating or maintaining sleep, or awakening early in the morning and being unable to return to sleep)
- » **Duration:** Symptoms present for at least 3 months.
- » Symptoms cause functional impairment or distress
- » Symptoms occur despite having enough time to sleep
- » **Not Better Explained By:** Another sleep disorder, substance use, or a coexisting mental disorder.



TREATMENT OF INSOMNIA

- » **Non-pharmacologic treatment:** Cognitive Behavioral Therapy for Insomnia (CBT-I)
 - » **Sleep hygiene:** Educate about good sleep practices (e.g., consistent sleep schedule, comfortable sleep environment, Regular exercise is beneficial but should be avoided 6 hours before bedtime, Quiet, dark, pleasantly cool bedroom and a comfortable bed, No large meals before bedtime.
 - » **Stimulus control:** Go to bed only when sleepy, get out of bed if unable to sleep within 20 minutes, use bed only for sleep and intimacy. Caffeinated drinks & nicotine should be avoided 3-4 hrs. before bedtime
 - » **Sleep restriction therapy:** Limit time in bed to the actual sleep time to increase sleep drive.
 - » **Cognitive therapy:** Address and reframe negative thoughts about sleep.

2. Pharmacologic treatment:

- » **Benzodiazepine Receptor Agonists:**
 - » Tab. Zolpidem 10mg (Stillnox, Zolp, Xolnon) x at dose 5-10mg orally before bedtime (HS)
 - » OR Tab. Eszopiclone 1mg, 2mg, 3mg (Clonexa) x at dose 1-3mg orally before bedtime (HS)
- » **Short acting benzodiazepine**
 - » OR Tab. Midazolam 7.5mg (Dormicum) at dose 7.5-15mg before bedtime (HS)
 - » OR Tab. Triazolam 0.250mg (Halcion) at dose 0.250mg (250 mcg) taken before bedtime (HS)
 - » OR Cap. Temazepam 15mg OR 30mg (Restoril) at dose 15-30 mg before bedtime (HS)
- » **OR Other medications:**
 - » **Sedating Antidepressants:** Effective especially if insomnia coexists with depression or anxiety.
 - » Tab. Trazodone 50mg OR 100mg (Deprel, Trazolam) at dose 25-100mg before bedtime (HS)
 - » OR Tab. Mirtazapine 15mg (Mirtazep) at dose 7.5-15mg
 - » OR Tab. Doxepin at dose 3-6 mg before bedtime (HS)
 - » **Melatonin Receptor Agonists:** Tab. Melatonin at dose 0.5-5mg OR Tab. Ramelteon at dose 8 mg before bedtime (HS)
 - » **Orexin Receptor Antagonists:** Tab. Suvorexant at dose 10-20 mg before bedtime (HS)
- » **Insomnia in Pregnancy:** doxylamine, diphenhydramine



ACUTE STRESS DISORDER

Definition: Distressing symptoms related to the traumatic event that last between 3 days to 1 month following the exposure. **Acute stress disorder** is a psychiatric diagnosis that may occur in patients after witnessing, hearing about, or being directly exposed to a traumatic event, such as motor vehicle crashes, acts of violence (e.g., military combat, sexual assault, robbery), work-related injuries, natural or man-made disasters, or sudden and unexpected bad news (e.g., diagnosis of life-threatening illness, death of a loved one).

DIAGNOSTIC CRITERIA (ACCORDING TO DSM-5)

- **Exposure to death (actual or threatened), injury, or sexual abuse that occurs in ≥ 1 of the following:**
 - » Direct experience of these events
 - » Witnessing these events
 - » Hearing about these events happening to close friends or family
 - » Repeated exposure to unpleasant details of traumatic events occurring to others
- **At least 9 of the following 14 symptoms are present:**
 - » **Intrusion**
 - 1) Recurrent distressing memories
 - 2) Recurrent distressing dreams
 - 3) Flashbacks
 - 4) Severe psychological distress or physiological responses to internal or external cues related to the event
 - » **Negative mood**
 - 5) Inability to feel positive emotions (e.g., happiness, satisfaction, or love)
 - » **Dissociation**
 - 6) Altered sense of reality
 - 7) Loss of memory with regards to important details of the event
 - » **Avoidance**
 - 8) Avoidance of memories, thoughts, or feelings related to the event
 - 9) Avoidance of external reminders (e.g., places, people, conversations, objects) related to the event
 - » **Arousal**
 - 10) Sleep disturbance
 - 11) Irritable behavior
 - 12) Hypervigilance
 - 13) Poor concentration
 - 14) Heightened startle reflex
- **Duration:** Symptoms last from 3 days to 1 month following the traumatic event.
- The affected individual has been experiencing significant distress or impaired social and/or occupational functioning since the traumatic event.
- Symptoms are not explained by substance misuse or another medical condition.



△ Acute stress disorder C/C:

Patients with Acute stress disorder respond with Intense fear, helplessness, or horror, and may report anxiety, depression, fatigue, headaches, and gastrointestinal and rheumatic symptoms.



- The management of acute stress disorder involves normalizing the patient's responses, providing psychological first aid, and monitoring the patient over time.
- **Acute treatment:** Inj. Diazepam 10mg/2ml (valium) x dilute in 8ml 0.9% NS x administer 4mg to 10mg slow IV
OR Inj. Inj Haloperidol 5mg (Serenace) + Inj Diazepam 10mg (Valium) x IM/IG x STAT
- Referral to a psychologist or psychiatrist may be necessary if symptoms worsen or persist.
- **Discharge patient on:** Tab. Clonazepam 0.5mg (Revotril, Naze) x HS
OR Tab. Alprazolam 0.5mg (Alp, Xanax) x HS

PANIC ATTACK

Panic attacks may be precipitated by situations known to be stressful, at least some attacks must be unexpected ("out of the blue"). Patients also exhibit anticipatory anxiety in which they experience ongoing psychic distress by worrying about their next panic attack or the attack's effects (e.g., humiliation if the attack were to happen in public view). In addition, patients manifest avoidance behavior by staying away from known triggers or from situations in which having a panic attack might be dangerous (e.g., driving) or particularly distressing (e.g., in public spaces). For many patients, the anticipatory anxiety and avoidance behavior may be more disabling than the panic attacks themselves.

△ Panic Attack

C/C:

- Episodes of intense fear and discomfort that last for several minutes
- Intense fear of dying
- Disconnectedness/loss of reality
- **Overstimulation of the sympathetic system**
 - Sweating, palpitations
 - Paresthesias, chest pain
 - Abdominal pain, nausea, light-headedness,
 - Shortness of breath (SOB), choking sensation

Investigation: CXR, ECG, Trop-I, TFTs,

Rx

For Acute Attack

1. Tab. Alprazolam 0.5mg or 1mg (Alp, Praz, Xanax)
OR Tab. Bromazepam 3mg (Relaxin, Lexotiniil)
0 – 0 – 1
2. If hyperventilation: Breathing in a paper bag

For Long-term management should be added

3. Tab. Escitalopram 5mg or 10mg (Estar, Pixnew)
OR Cap. Fluoxetine 20mg (Prozac, Flux, Depex)
1 – 0 – 0 (One tab after breakfast)
ایک گولی صبح ناشتے کے بعد

PANIC DISORDER

△ Panic Disorder

C/C:

- 4 or more panic attacks in a 4-week period, or ≥1 panic attacks followed by at least 1 month of fear of another panic attack
- **Panic attack symptoms may include:**
 - Intense fear of dying
 - Disconnectedness/loss of reality
 - **Overstimulation of the sympathetic system**
 - Sweating, palpitations
 - Paresthesias, chest pain
 - Abdominal pain, nausea, light-headedness,
 - shortness of breath (SOB), choking sensation
- Panic attack symptoms have no precipitating stimulus and often peak within 10 minutes and last 20-30 minutes from onset
- Panic attacks may be triggered by injury, illness, interpersonal conflict or loss, cannabis use, or stimulants (caffeine or decongestants)

Rx

1. Cognitive Behavioral Therapy (CBT)
2. Tab. Alprazolam 0.5mg (Alp, Praz, Xanax)
OR Tab. Bromazepam 3mg (Relaxin, Lexotiniil)
0 – 0 – 1 (HS)
Benzodiazepines (Alprazolam, Bromazepam) may be used until antidepressants take effect.
3. Tab. Escitalopram 5mg or 10mg (Estar, Citanew)
OR Cap. Fluoxetine 20mg (Prozac, Flux, Depex)
1 – 0 – 0 (One tab after breakfast)
ایک گولی صبح ناشتے کے بعد



GENERALIZED ANXIETY DISORDER (GAD)

- Definition: an anxiety disorder in which patients have anxiety that is prolonged, excessive, persistent (> 6 months), and caused by various aspects of daily life instead of a single specific situation or object
- Epidemiology
 - » Most common anxiety disorder among the elderly population
 - » Lifetime prevalence: 5–10%
 - » Sex: Female > male (2:1)
- Associated conditions: Major depressive disorder, Substance misuse disorders

△ GAD

C/C:

Clinical features:

Diagnosis is confirmed if the following symptoms occur more days than not for at least 6 months.

- » Excessive anxiety and persistent worrying
- » At least 3 of the following
 1. Restlessness/Nervousness
 2. Fatigue
 3. Difficulty concentrating
 4. Irritability
 5. Muscle tension
 6. Sleep disturbance
 7. Concentration difficulties.

Olanzapine may causes hyperglycemia and hyperlipidemia, should be monitor with FBS, HBA1C and Fasting lipid profile.

Management of GAD

- First-line treatment: psychotherapy, pharmacotherapy, or both
 - » Psychotherapy: refer to psychologist
 - Cognitive behavioral therapy (CBT)
 - Applied relaxation therapy
 - Biofeedback
 - » Pharmacotherapy: SSRIs or SNRI for at least 12 months
- Second-line treatment: TCAs, Benzodiazepines, Buspirone
- Note: Benzodiazepine can be used until SSRIs take effect but should never be used for long-term management, as they increase the risk of benzodiazepine dependence
- For refractory cases: Antipsychotics (Olanzapine, Risperidone)

Rx

Selective serotonin reuptake inhibitors (SSRIs)

1. Cap. Fluoxetine 20mg (Prozac, Flux, Depex)
OR Tab. Escitalopram 5mg or 10mg (Estar, Citanew)
OR Tab. Paroxetine 12.5mg or 25mg (Paraxyl, Seroxat)
1-0-0 (One tab after breakfast)
ایک گولی صبح ناشتے کے بعد (SNRIs)

Alternative: Serotonin-norepinephrine reuptake inhibitors

- Tab. Venlafaxine (Effexor XR, Enpress, Vendep)
 - » Available strength: 37.5mg or 75mg or 150mg
 - » Maximum dosage: 150 mg to 225 mg
 - » Start from low dose (37.5mg upto 75mg) x at bedtime

Benzodiazepine

2. Tab. Alprazolam 0.5mg or 1mg (Alp, Praz, Xanax)
OR Tab. Clonazepam 0.5mg or 2mg (Revotril, Naze)
OR Tab. Bromazepam 3mg (Relaxin, Lexotinil, Bromalex)
0-0-1

Rx

Alternative or for severe cases

1. Cap. Olanzapine 3mg or 6mg or 12mg + Fluoxetine 25mg
Available brand: Co-Depicap, Dipof, Olanzagel
Available strength: 3/25mg, 6/25mg, 12/25mg
Cap. Co-Depicap 3/25mg
OR Cap. Co-Depicap 6/25mg
OR Cap. Co-Depicap 12mg/25mg
0-0-1 (HS)

MAJOR DEPRESSIVE DISORDER (MDD)

- Definition: Major depressive disorder (MDD) is an episodic mood disorder primarily characterized by depressed mood and anhedonia lasting for at least two weeks.
- Sex: women > men, the average age of onset is 30 years

DIAGNOSTIC CRITERIA ACCORDING TO DSM-V FOR MAJOR DEPRESSIVE DISORDER (MDD)

- Five or more of the nine symptoms listed below, for at least 2 weeks, with at least one of the symptoms being depressed mood or anhedonia
 - Depressed mood for most of the day, almost every day (in children, can manifest with irritability)
 - Sleep disturbance (insomnia or hypersomnia)
 - Anhedonia:** an inability to enjoy acts or experiences that are normally pleasurable.
 - Feelings of worthlessness or disproportionate guilt
 - Fatigue or loss of energy
 - Diminished concentration, cognition, and ability to make decisions (pseudo-dementia)
 - Weight change due to appetite change
 - Psychomotor changes (observed by others)
 - » Agitation
 - » Retardation
 - Suicidal ideation:** Suicidal **thoughts** a preoccupation with ending one's own life.
- There is clinically significant distress or impaired functioning in important areas of life (e.g., work, school).
- Symptoms are not due to the effects of psychoactive substances or organic disease.
- Symptoms are not superimposed upon or due to schizoaffective disorder or another psychotic disorder.
- There is no history of a manic or hypomanic episode.
- Criteria A-C are met: Major depressive episode (MDE)
- Criteria A-E are met: Major depressive disorder (MDD)

SEVERITY (ACCORDING TO DSM-V)

- Treatment recommendations are often categorized by severity:
 - Mild major depressive disorder (MDD):** minimal number of symptoms to fulfill diagnostic requirements PLUS manageable symptom intensity PLUS minor impaired functioning
 - Moderate major depressive disorder (MDD):** number of symptoms, symptom intensity, and impaired functioning greater than "mild" but less than "severe"
 - Severe major depressive disorder (MDD):** number of symptoms more than fulfill diagnostic requirements PLUS unmanageable symptom intensity PLUS extremely impaired functioning

ASSESSMENT FOR THE EXCLUSION OF ORGANIC CAUSES

- Comprehensive history and physical examination**
 - » Assess patients for features of physical diseases that mimic depression, e.g., features of hypothyroidism.
 - » **Screen for medication-induced depressive disorder:** e.g., beta blockers, steroids, oral contraceptives
- Routine blood test:** Serum TSH (TFTs), CBC, Vitamin B12, Folate, BUN, Creatinine, Electrolytes
- Consider the following based on clinical suspicion:**
 - » Serum and urine toxicology
 - » HIV testing
 - » Syphilis screening
 - » Diagnostic studies for Lyme disease
 - » Testosterone levels (in male)
- CT scan/MRI brain:** Consider evaluating for structural brain disease based on clinical presentation.
- Cognitive testing:** to assess for memory issues and dementia



TREATMENT APPROACH IN PATIENT WITH MDD

- ☞ Advise patients on lifestyle modifications.
- ☞ **Start initial treatment based on severity.**
 - » **Mild depression:** typically psychotherapy alone & the passage of time. do not require medication therapy
 - » **Moderate and severe depression:** Psychotherapy and Medication therapy
 - » **Psychotic depression** should be treated with a combination of an antipsychotic & an antidepressant (SSRI)
- ☞ **Refer urgent:** Patients with severe/complex depression or suicidality to psychiatry; admission may be required
- ☞ Provide the patient and their family with information on depression.
- ☞ **Ensure patients receive treatment for:**
 - » **Psychiatric comorbidities:** Panic, alcohol use disorder, generalized anxiety disorder (GAD), substance use
 - » Contributing physical conditions
- ☞ Review patients regularly; assess the efficacy of treatment at = 6 weeks and consider modifications.

STARTING OF PHARMACOTHERAPY IN PATIENT WITH MAJOR DEPRESSIVE DISORDER (MDD)

- ☞ **Initiation medication therapy**
 - **Choice of initial medication**
 - » Most antidepressants have comparable efficacy but different adverse effects.
 - » **When choosing an antidepressant, consider:** Psychiatric and medical comorbidities, current symptoms, Previous treatment experiences, drugs adverse effects and Interactions with other drugs
 - **Starting of initial medication trial**
 - » Typically requires ≥4 weeks to take effect
 - » Start with the lowest dose and increase slowly (e.g., with dose adjustments every 2 weeks).
 - » **Monitoring:** During the medication trial, patients should be monitored for worsening mood, manic symptoms, psychotic symptoms, agitation and suicidal ideation, every 1–2 weeks until week 6
- ☞ **First-line antidepressant medications**
 - Options include SSRIs (often trialed first), SNRIs, and the atypical antidepressants, bupropion & mirtazapine.
 - For further information on adverse effects and contraindications.

△ **Major depressive disorder (MDD)**

C/C:

- ☞ Depressed mood
- ☞ **Anhedonia**
- ☞ Feelings of guilt
- ☞ Worthlessness, or hopelessness
- ☞ Low energy levels
- ☞ Difficulty concentrating
- ☞ Changes in appetite and weight (↑ or ↓)
- ☞ Sleep disorders (insomnia or hypersomnia)
- ☞ Psychomotor agitation or retardation
- ☞ **Suicidal thoughts**
- ☞ **May additionally manifest with:**
 - » **Somatic features:** headaches, myalgia, gastrointestinal problems
 - » Aggression, substance use disorder, or increase in risk-taking behavior

SIGECAPS mnemonic for depression features:

- ☞ **S**leep (insomnia or hypersomnia)
- ☞ **I**nterest loss (anhedonia)
- ☞ **G**uilt (low self-esteem)
- ☞ **E**nergy (low energy or fatigue)
- ☞ **C**oncentration (poor concentration or difficulty making decisions)
- ☞ **A**ppetite (decreased appetite or overeating)
- ☞ **P**sychomotor agitation or retardation, and
- ☞ **S**uicidal ideation.

Rx

- ☞ **Advice lifestyle modifications**
 - » Sleep hygiene
 - » Reduction in substance use, alcohol, recreational drugs
 - » Stress reduction and Relaxation/mindfulness
 - » Increasing social support
 - » Regular aerobic exercise
 - » Improved nutrition
- ☞ **Psychotherapy:** May be used alone or along with medicines
 - » Cognitive behavioral therapy (CBT)
 - » Interpersonal therapy
 - » Behavioral activation
 - » Psychodynamic psychotherapy
 - » Supportive psychotherapy
- ☞ **First-line drugs for major depressive disorder (MDD)**
 - » **SSRIs:** Fluoxetine, Escitalopram, Paroxetine, Sertraline
 - » **SNRIs:** Venlafaxine, Desvenlafaxine, Duloxetine
 - » **Atypical antidepressants:** Bupropion, Mirtazapine
 - » **Other antidepressant medication** which causes more adverse effects than first-line therapies such as SSRIs.
- ☞ **Options include:**
 - » **Trazodone:** used primarily for insomnia; a higher dose is required when used as an antidepressant
 - » **Tricyclic antidepressants:** Amitriptyline, Nortriptyline
 - » **Monoamine oxidase inhibitors (MAOIs):** Phenelzine

TREATMENT OF MAJOR DEPRESSIVE DISORDER (MDD)

- » Advise patients on lifestyle modifications (explained above).
- » Provide the patient and their family with information on depression.
- » Advise Psychotherapy, refer the patient to Psychotherapist/Psychologist
- » Antidepressants therapy

» Selective serotonin reuptake inhibitors (SSRIs)

- » Tab. Escitalopram 10mg or 20mg (Cipralext, Estar, Citanew) x 10–20 mg PO once daily in the morning
- » OR Cap. Fluoxetine 20mg (Flux, Prosac, Depex) starting at 20–80 mg PO once daily in the morning
- » OR Tab. Paroxetine 20mg (Seroxate, Paraxyl, Paroxin) 10–50 mg PO once daily at bedtime
- » OR Tab. Sertraline 50mg or 100mg (Sert, Freedep, Serlin) x starting at dose 25mg orally once daily and increasing gradually up to 100 – 200mg depending on response.
- » OR Tab. Fluvoxamine 50mg or 100mg (Faverin, Voxamine) 50 – 300mg PO once daily at bedtime
- » OR Tab. Citalopram 20mg (Cipram, Citalo, Lexapram) 20–40 mg PO once daily

» OR Selective serotonin norepinephrine reuptake inhibitors (SNRIs)

- » OR Tab. Venlafaxine XR (extended release) x starting at dose 37.5 mg orally once daily and titrated gradually as indicated to a maximum dose of 225mg/day
- » OR Tab. Desvenlafaxine 50mg PO once daily
- » OR Tab. Duloxetine 60mg PO once daily or 30 mg PO twice daily

» OR Atypical antidepressants:

- » OR Tab. Bupropion XR (extended release): initial dose 150 mg PO once daily for the first 3 days then increase to 300 mg once daily.
- » OR Tab. Mirtazapine 15–45 mg PO once daily at bedtime
- » OR Tab. Vortioxetine 10mg OD, orally and may be increased to 20mg/day

SWITCHING OR DISCONTINUING ANTIDEPRESSANTS

- » When switching between antidepressants, consider medication class and the risk of serotonin syndrome.
 - » From one SSRI (excluding fluoxetine) to another SSRI or SNRI: usually a direct switch
 - » To or from non-MAOI classes: usually cross taper
 - » To or from an MAOI: Taper completely, followed by a 2–6 week washout period.
- » When discontinuing medications:
 - » Consider tapering over 6–8 weeks to:
 - Decrease the risk of relapse
 - Prevent antidepressant discontinuation syndrome
 - » Offer psychotherapy to prevent relapse
- » When changing between antidepressants, monitor patients carefully for the features of serotonin syndrome.
- » Symptoms of antidepressant discontinuation syndrome occur when treatment is **FINISHED**: Flu-like symptoms, Insomnia, Nausea, Imbalance, Sensory disturbances, Hyperarousal

TREATMENT-RESISTANT DEPRESSION

- » Definition: Major depressive disorder (MDD) that persists despite trials of ≥ 2 antidepressants at optimal doses
- » Should not be diagnosed without assessing patients for:
 - Comorbid psychiatric conditions: Anxiety, Panic, substance use disorder, Panic, alcohol use disorder
 - Adherence to antidepressant therapy
- » Management of Treatment-resistant depression
 - Refer all patients to a psychiatrist to determine further treatment.
 - Augmenting agents for depression such as: Bupropion (150–450 mg/day), lithium (300–900 mg/day orally), thyroid medication (Liothyronine, 25–50 mcg/day per orally), or a second generation antipsychotic (Aripiprazole 5–15 mg/day), Anticonvulsant mood stabilizers (Lamotrigine)
 - Neurostimulation therapy
 - » Electroconvulsive therapy (ECT)
 - Highly effective treatment for treatment-resistant MDD and severe MDD
 - Accessibility and patient acceptance have limited its use.
 - Requires regular attendance for intensive therapy followed by a gradual taper
 - » Vagal nerve stimulation
 - » Transcranial magnetic stimulation



OBSESSIVE-COMPULSIVE DISORDER (OCD)

- Definition: OCD is characterized by persistent and recurring thoughts, urges, or images (obsessions) that lead to repetitive behaviors or mental acts (compulsions). Since obsessions are experienced as intrusive and involuntary as well as undesirable and unpleasurable, they generally cause anxiety or distress.
- Sex: Male-to female ratios are similar, with the highest rates occurring in the young, divorced, separated, and unemployed (all high stress categories). The average age of onset is 20 years.

CLINICAL FEATURES

- Ego-dystonic: Behavior or thought patterns that are inconsistent with or repulsive to one's sense of self
 - Opposite of ego-syntonic
 - Behavior patterns are in agreement with one's sense of self
 - Seen in obsessive-compulsive personality disorder
- Obsessions: Distressing thoughts, emotions, and/or sensations that are recurring and intrusive.
- Compulsions: Repetitive actions to provide relief from anxiety caused by obsessions (can take up a substantial amount of time)
- Comorbidities: Anxiety disorders, Depressive disorders, Bipolar disorders, Tic disorders, Tourette syndrome, Personality disorders and Schizophrenia or Schizoaffective disorder

OCD DIAGNOSTIC CRITERIA (DSM-V)

- Obsessions (کسی وہم کا ذہن میں بس جاتا/وہم کا غلبہ) and/or Compulsions (شدید خوابش):
 - Obsessions (e.g., thoughts about contamination, harm, or symmetry) defined by both:
 - Recurrent/persistent, intrusive thoughts, or urges that cause anxiety or distress
 - Attempts to suppress these thoughts or urges
 - Compulsions (e.g., repeatedly washing hands, opening and closing a door multiple times, or rearranging objects on a desk) defined by both:
 - Repetitive behaviors or mental exercises (e.g., counting, repeating words) that the individual feels compelled to perform in order to relieve anxiety brought upon by the obsessions.
 - These behaviors or mental actions may be performed in an attempt to prevent some perceived dreaded event, though they tend to be excessive and not connected in any realistic way to the event.
- Time-consuming (for example ≥ 1 hour/day), or result in significant distress/impairment (school, work)
- Not due to substance-use disorders or another medical condition
- Not due to another mental disorder (e.g., anxiety disorders, eating disorders)

Guidelines: ADAA, Oxford textbook of psychiatry, CMDT-23, Prescribe guidelines in psychiatry – The Maulvi

Rx

TREATMENT OF OBSESSIVE-COMPULSIVE DISORDER (OCD)

A COMBINATION OF PHARMACOTHERAPY & PSYCHOTHERAPY IS EFFECTIVE IN THE TREATMENT OF OCD

- Cognitive-behavioral therapy (CBT)
 - Cognitive therapy techniques
 - Exposure and response prevention
- Pharmacotherapy with antidepressants or/and atypical antipsychotics (if psychotic features)
 - Preferred antidepressants in OCD with SSRIs, continue at least for 8 – 12 weeks is needed, including 4 to 6 weeks or several months' treatment is often needed to achieve a maximum response.
 - Cap. Fluoxetine 20mg (Flux, Prozac, Depex) initially starting at 20mg orally once daily in the morning, titrated up to 60–80 mg. Fluoxetine widely used but in doses higher than those used in depression.
 - OR Tab. Fluvoxamine 50mg or 100mg (Faverin, Voxamine) x at dose 100–300mg PO OD at bedtime
 - OR Tab. Sertraline 50mg or 100mg (Sert, Freedep, Serlin) x starting at dose 25mg orally once daily and increasing gradually up to 100 – 200mg depending on response.
 - OR Tab. Paroxetine 20mg (Seroxate, Paraxyl, Paroxin) x at dose 20mg up to 40 mg OD at bedtime
 - Alternative: Tricyclic antidepressants with serotonergic action: Tab. Clomipramine 25mg (50–225mg/day)
 - If not response after 10 – 12 weeks therapy or patient with features with psychosis, consider atypical antipsychotics alone or low doses in combination with SSRIs:
 - Tab. Risperidone 1mg or 2mg (Risp, Buzon, Risperdal) initially at dose 0.5mg, up to 1–3mg x OD
 - Tab. Aripiprazole 10mg (Aripip, Profy, Adablizer) x initially at dose 5mg, up to 10–15mg x at morning

BIPOLAR AFFECTIVE DISORDER (BIPAD)

- Definition: Bipolar disorder is a psychiatric condition characterized by episodes of mania (or hypomania) and major depression, interspersed with periods of normal mood and functioning.
- Sex: Men and women are equally affected, the average age of onset is 20 years

ETIOLOGY

- Multifactorial origin
 - Strong genetic component → increased risk if first-degree relative is affected
 - Increased paternal age → ↑ mutations during spermatogenesis → ↑ risk of bipolar disorder in offspring
- Precipitating factors: Psychosocial stress, Drugs (Dexamethasone, Phencyclidine, Amphetamine, Cocaine, Benzodiazepines), Alcohol, Childhood traumatic experiences, Sleep disturbances and Physical illness

CLINICAL FEATURES

- Generally bipolar disorder is characterized by alternating episodes of mania (often also hypomania) and major depression, in between which individuals may be asymptomatic.

Manic/hypomanic episode

- Characterized by an elevated mood
- Symptoms include:
 - Intense prolonged happiness (e.g., for several days)
 - Irritability
 - Overconfidence, risky behavior (e.g., overspending money)
 - Decreased need for sleep
 - Hypersexuality
 - Psychotic features

Major depressive episode

- Characterized by a depressed mood
- Symptoms include:
 - Anhedonia
 - Fatigue
 - Sleep disturbances
 - Frequent reports of pain (headache, stomach ache)
 - Lack of interest in activities that were previously enjoyed
 - Feelings of worthlessness or guilt
 - Suicidal ideation

- To remember the features of a manic episode, think: "DIG FAST": Distractibility, Irresponsibility, Grandiosity, Flight of ideas, Activity increase, Sleep deficit, and Talkativeness.
- SIGECAPS for features of depression: Sleep (insomnia or hypersomnia), Interest loss (anhedonia), Guilt (low self-esteem), Energy (low energy or fatigue), Concentration (poor concentration or difficulty making decisions), Appetite (decreased appetite or overeating), Psychomotor agitation or retardation, and Suicidal ideation.

TYPES OF BIPOLAR DISORDER

- Bipolar-I disorder: at least one episode of mania. Major depressive or hypomanic episodes usually occur but are not required for diagnosis.
- Bipolar-II disorder: at least one episode of hypomania and one major depressive episode; no previous episodes of mania (distinguishing feature from bipolar-I)

DSM-V DIAGNOSTIC CRITERIA FOR MANIC & HYPOMANIC EPISODES

	MANIC EPISODE	HYPOMANIC EPISODE
Core definition	Abnormally elevated, expansive, or irritable mood and increased goal-directed behavior not attributable to an organic psychic disorder or psychotropic substances	
Duration	Most of the day for at least 1 week	Most of the day for at least 4 consecutive days
Criteria	≥ 3 of the following: - Increased goal-directed activity (sexually, at work, and/or socially) or psychomotor agitation - Increased talkativeness or pressure of speech - Flight of ideas or racing thoughts - Loss of social inhibitions - Hedonistic, socially inappropriate, and reckless behavior	



	6. Aggressiveness, hostility 7. Decreased need for sleep 8. Heightened self-esteem or grandiosity 9. Distractibility	
Extent of dysfunction	Significant dysfunction (work/school), patient requires hospitalization (risk of harm to self or others), or presence of psychotic features	Does not result in significant dysfunction, hospitalization, or manifests with psychotic features
☞ The DSM-5 diagnostic criteria are used to identify episodes of mania, hypomania, and major depression. » Bipolar-I disorder: ≥1 confirmed episode of mania » Bipolar-II disorder: ≥1 confirmed episode of hypomania AND ≥1 major depressive episode AND absence of any manic episodes.		

DSM-V DIAGNOSTIC CRITERIA FOR MAJOR DEPRESSIVE EPISODE

Core definition	☞ A change in usual function that is characterized by depressed mood and/or anhedonia, accompanied by other related symptoms, and not attributable to psychoactive substances, organic disease, or significant loss
Duration	☞ Symptoms are present almost every day, for at least 2 weeks.
Criteria	☞ ≥ 5 of the following: 1. Depressed mood lasting for most of the day 2. Sleep disturbance (insomnia or hypersomnia) 3. Loss of interest or anhedonia 4. Feelings of worthlessness or guilt 5. Fatigue or loss of energy 6. Diminished concentration or ability to make decisions 7. Significant change in weight (not associated with dieting) or appetite 8. Psychomotor changes (agitation or retardation) 9. Recurrent suicidal ideation or thoughts of death ☞ At least one of the symptoms must be depressed mood or anhedonia.
Extent of dysfunction	☞ Clinically significant distress or impaired functioning in important areas of life (e.g., work, school)
☞ Major depression criteria: ≥5 symptoms, for at least 2 weeks, with at least one of the symptoms being depressed mood or anhedonia	

DIAGNOSTIC WORKUP

Investigations help rule out differential diagnoses and detect conditions that may affect management. A complete history and physical examination should guide the requested studies.

☞ Blood test

- » CBC (may detect anemia)
- » BUN, creatinine, electrolytes, LFTs: to establish a baseline before long-term pharmacological treatment
- » Thyroid function tests (Serum TSH): to rule out thyroid disease
- » Additional blood test: based on the suspected underlying condition
- » Monitoring studies depend on medications (e.g., serum levels of lithium or valproate, liver chemistries)

☞ Urine

- » Urinalysis: may identify urinary tract infections
- » Urine toxicology screen: to rule out acute intoxication (e.g., with amphetamines)
- » Pregnancy test: Pregnancy will affect treatment decisions.

☞ ECG: To identify QT interval prolongation that may be aggravated by lithium, valproic acid, and antipsychotics

MANAGEMENT OF BIPAD

☞ General principles

- » Consult with psychiatrist/psychiatry department before starting treatment.
- » Goals

- **Acute treatment:** Resolution of mania and psychosis (if present) in order to prevent harm to the patient and/or others
- **Maintenance therapy:** Prevention of manic episodes, reduction of suicide risk, improvement in social functioning
- **Effective treatment combines pharmacotherapy with psychological interventions** (e.g., cognitive behavioral therapy).
- **Severe mania - Mood stabilizer (Lithium or Valproate) PLUS Antipsychotic**
 - If a patient does not respond to medication within 1–3 weeks, continue with the antipsychotic and switch lithium to Valproate or Carbamazepine or Lamotrigine
 - If a patient is still not responsive, switch the antipsychotic to another antipsychotic drug.
 - If a patient has refractory mania, discontinue pharmacotherapy and switch to ECT.
- **Mania/hypomania in pregnancy:** typical antipsychotics (haloperidol) OR ECT (if severe or refractory mania)
- **Management of agitation:** Rapid-acting intramuscular atypical antipsychotics (Olanzapine, aripiprazole) or benzodiazepines (Diazepam, lorazepam)



TREATMENT FOR ATTACK (AGGRESSIVE, AGITATED, UNEASY BEHAVIORS) IN EMERGENCY

1. Inj. Haloperidol 5mg//ml (Serenace) x IM x STAT
 2. PLUS Inj. Diazepam 10mg/2ml (Valium) x IM or IV diluted x STAT
- Acute mania is considered a psychiatric emergency and requires immediate management. The goal of acute treatment is resolution of mania and psychosis (if present) as well as preventing any harm to the patient or others.
 - Inj Fluphenazine 25mg (Flucate) x monthly for recurrent and chronic patients



PRESCRIPTION OF MILD TO MODERATE MANIA

1. Tab Lithium monotherapy 400mg (Neurolith SR, Lithotrop SR) Or Tab. Olanzapine 5mg, 10mg (Olanza, Olipro) 1–0–1 (BD)
2. Tab Lorazepam 1mg, 2mg (Ativan, Tenzil) Or Tab. Clonazepam 0.5mg, 2mg (Revotril, Naze) x OD



PRESCRIPTION OF SEVERE MANIA

1. Tab. Sodium Valproate 250mg, 500mg (Epival, Dapakan) Or Tab Carbamazepin 200mg (Tegrol, Terol, Seizunil) 1–0–1 (BD)
2. Tab. Haloperidol 1.5mg, 5mg, 10mg (Serenace, Dosik) Or Tab. Risperidone 1mg, 2mg, 3mg, 4mg (Risp, Buzon) 1–0–1 (BD)
3. Tab. Procyclidine 5mg (Kamadrin, Kampro) x OD/BD for Extra-pyramidal syndrome (EPS)
4. Tab. Lorazepam 1mg, 2mg (Ativan, Tenzil) Or Tab. Clonazepam 0.5mg, 2mg (Revotril, Naze) x HS/BD



PRESCRIPTION OF REFRACTORY OR SEVERE BIPOLAR EPISODES

1. Consider electroconvulsive therapy (ECT)
2. No response to initial treatment: Change the choice of mood stabilizer and/or antipsychotic.
 - Tab Lithium monotherapy 400mg (Neurolith SR, Lithotrop SR) x OD
 - OR Tab. Sodium Valproate 250mg or 500mg (Epival, Dapakan) x BD
3. Tab. Olanzapine 5mg or 10mg (Olanza, Olipro) OR Tab. Risperidone 1mg, 2mg, 3mg or 4mg (Risp, Buzon) x BD
4. Tab. Lorazepam 1mg or 2mg (Ativan, Tenzil) OR Tab. Clonazepam 0.5mg or 2mg (Revotril, Naze) x HS/BD



PRESCRIPTION OF SEVERE DEPRESSION OR PREDOMINANTLY DEPRESSIVE BIPOLAR-II DISORDER

- Antidepressants may be started after initiating mood stabilizers. Avoid prescribing antidepressants to patients with bipolar disorder before initiating therapy with mood stabilizers, as antidepressants can precipitate a manic episode.
1. Cap. Fluoxetine 20mg (Prozac, Flux, Depex) x 1–0–0 (OD)
 2. Tab. Risperidone 1mg or 2mg or 3mg or 4mg (Risp, Risperdal, Buzon) x 1–0–1 (BD)
 3. Tab. Lorazepam 1mg or 2mg (Ativan, Tenzil) x HS/BD



SCHIZOPHRENIA

- ☛ **Definition:** Schizophrenia usually involves delusions (false beliefs), hallucinations (seeing or hearing things that don't exist), unusual physical behavior, and disorganized thinking and speech.
- ☛ **Risk factors**
 - » **Family history:** risk significantly increased if close relatives are also affected
 - » **Psychological stress**
 - » **Cannabis use:** Heavy marijuana use during early teens (associated with increased incidence and worse course of positive symptoms)
 - » **Advanced paternal age (father age) at conception**

CLINICAL FEATURES

☛ **Positive symptoms**

- » **Hallucinations:** Auditory (sound) hallucinations are most common in schizophrenia – it may be perceived as either inside or outside the patient's brain; they are usually described as hearing voices, command, derogatory, conversing, and/or running commentaries. Visual (sight), olfactory (smell), and gustatory (taste) hallucinations also occur but are less common. **Tactile hallucinations** (touching, electrical pulses, and crawling sensation) rarely present in schizophrenia and should prompt suspicion of drug-induced psychosis.
- » **Delusions:** a collection of **fixed, false beliefs** not attributable to a patient's culture or religion that are maintained despite being contradicted by reality or rational arguments
- » **Disorganized thought processes:** Disorganized speech, behavior and trouble with thinking
 - **Pressured speech:** this refers to rushed intense speech.
 - **Incongruent affect:** this refers to disconnect between thought and speech content.
 - **Tangential speech:** this refers to an inability to stay on topic, jumping from one subject to another and does not appropriately answer a question).
 - **Loose association:** this refers to the complete incoherence and disorganized thought expressed verbally through rapid and dissociated switching from one topic to the next (e.g., "I took my mother shopping but the sun was so bright because the door was shut.").
 - **Verbigeration:** a repetition of words in the absence of stimuli.
 - **Perseveration:** a repetition of the same response (e.g., word or phrase) to different stimuli.
 - **Word salad:** a speech form in which no connection between words is found. For example "Over the moon, ocean yellow a cabinet runs circle").

☛ **Negative symptoms**

- » **Flat affect:** reduced or absent emotional expression
- » **Social withdrawal:** a loss of drive for social interactions
- » **Anhedonia:** decreased ability to experience pleasure
- » **Lack of motivations (Avolition):** decreased motivation to self-initiate purposeful activities (e.g., the patient may sit for long periods of time and show little interest in participating in work or social activities).
- » **Alogia:** Lack of speech or thought
- » **Grossly catatonic behavior:** characterized by abnormal movements and reactivity to the environment

☛ **Cognitive impairment:** Inattention, impaired memory, poor executive functioning☛ **Affective disturbance**

- » **Inappropriate affect** (e.g., laughing in the absence of an appropriate stimulus)
- » **A dysphoric mood state** that can take the form of depression, anxiety, or anger
- » **Disturbed sleep patterns** (e.g., daytime sleeping, nighttime activity)
- » **Food refusal or a lack of interest in eating.**

☛ **Cultural considerations**

- » When interpreting symptoms, cultural and socioeconomic factors should be considered, particularly when the patient and the clinician do not share a cultural and/or socioeconomic background.
- » Ideas that appear to be delusional in one cultural context (e.g., evil eye, causing illness through curses, influences of spirits) may be commonly held in others. Visual or auditory hallucinations with a religious content (e.g., hearing God's voice) may be an expected component of some religious experiences.

- ☛ **Mood symptoms and anxiety:** Depression mostly, **other:** social or specific phobia, PTSD, OCD, Panic disorder



DIAGNOSTIC WORKUP

- » Schizophrenia is a clinical diagnosis based on the DSM-5 criteria.
- » Refer the patient to psychiatry department or consult psychiatrist urgently.
- » Investigations should be performed to rule out organic cause and before initiating pharmacological treatment
- » **MRI brain > CT scan brain:** Normal in schizophrenia; not routinely requested unless there are neurologic abnormalities or late onset, may be indicated on the basis of neurologic examination or history
- » **ECG:** Assess for potential QTc prolongation or evidence of cardiovascular disease.
- » **Laboratory test:**
 - » **Complete blood count (CBC):** Normal in schizophrenia, should be performed to screen for anemia
 - » BUN, creatinine, electrolytes, LFTs, TSH → normal in schizophrenia, to rule out organic cause
 - » **In female:** Pregnancy test for women of childbearing age
 - » Fasting blood glucose, HBA1C, and fasting lipid profile (alongside screening for diabetes risk factors)
 - » Prolactin, to screen for hyperprolactinemia, if indicated on the basis of clinical history.

SCHIZOPHRENIA DIAGNOSTIC CRITERIA

- » Diagnostic criteria include (according to DSM-5):
 - » At least 2 of the following symptoms, at least 1 of which is from the top three:
 1. Delusions
 2. Hallucinations
 3. Disorganized speech and behavior
 4. Grossly disorganized or catatonic behavior
 5. Negative symptoms
 - » The above symptoms persist for ≥ 1 month over a period of ≥ 6 months.
 - » Symptoms must cause social, occupational, or personal functional impairment lasting ≥ 6 months.
 - » Schizoaffective disorder and mood disorder with psychotic features have been ruled out.
 - » Medical or substance use disorder has been ruled out.

TREATMENT OF SCHIZOPHRENIA

- » Provide adjunctive non-pharmacological interventions to all patients.
 - » **Cognitive-behavioral therapy:** improves the quality of life and reduces positive symptoms
 - » **Psychoeducation:** associated with improved social functioning and lower relapse rates
 - » **Cognitive remediation therapy** in patients with cognitive impairment and **Social skills training**
 - » **Supported employment services:** improves employment outcomes
 - » Consider assertive community treatment in patients who are at ongoing risk of hospitalization, incarceration, and/or unstable housing
- » **Family interventions: reduce core symptoms and relapse rates**
 1. **Tab. Risperidone 1mg** (Risp, Risperdal) initially at dose 1mg orally twice daily, increase gradually according to response, maximum 16 mg/day (**Available doses:** 1mg, 2mg, 3mg or 4mg)
OR **Tab. Olanzapine 5mg or 10mg** (Olanza, Olipro) initially at dose 5mg orally once daily, increase gradually according to response to 10mg, maximum 20 mg/day
 2. **Control the extrapyramidal side effects:** **Tab. Procyclidine 5mg** (Kamadrin, Kampro) x OD/BD
 3. **For sleep disturbance/anxiety:** **Tab. Clonazepam 0.5mg or 2mg** (Revotril, Naze) x initially at dose 0.25mg to 0.5mg orally twice daily, increase gradually according to response, maximum 4 mg/day

Treatment resistant/refractory schizophrenia

(No response to 2 other antipsychotics/Persistent aggressive behavior or suicidal intentions)

1. **Tab. Clozapine 25mg, 100mg** (Saveril, Clozaril) x at dose 12.5mg BD gradually increase up to 300-350mg
 Enrollment in a national patient registry and frequent monitoring of clozapine levels
 CBC with absolute neutrophil count due to risk of fatal agranulocytosis are mandated for clozapine use
 - » For patients whose neutrophils remain within the normal range ($ANC > 1500/mcL$): First 6 months: weekly, At 6-12 months: every 2 weeks, After 12 months: monthly
 - » For patients with neutropenia: Moderate ($ANC 500-900/mcL$): three times weekly until within the normal range, Severe ($ANC < 500/mcL$): daily until within the moderate range
2. **Tab. Folic acid 5mg** x once daily



OPIOID USE DISORDER (OUD)

Clinical features

- » **Flu-like symptoms:**
 - Rhinorrhea, sneezing
 - Chills, headache
 - Piloerection, body itching
 - Myalgia, arthralgia, Leg cramps
- » **Gastrointestinal complaints:**
 - Nausea, vomiting
 - Abdominal pain/cramps
 - Diarrhea, constipation, weight loss
 - Hyperactive bowel sounds
- » **Features of sympathetic hyperactivity:**
 - Mydriasis (dilated pupils)
 - Tachycardia, arrhythmia
 - Hypertension
 - Hyperreflexia
- » **Features of CNS stimulation:**
 - Depressed or dysphoric mood, anxiety
 - Opioids craving, or a strong desire or urge
 - Hypersomnia (initial phase) or insomnia
 - Yawning, slurred speech
 - Irritability, Agitation
 - Aggressive behaviour
 - Memory impairment, confusion, seizures
- » **Other Factors:** sedation, hot and cold flashes, excess perspiration or lacrimation, shallow/slow respirations or apnea, needle marks, scars, or necrosis on skin near veins.

Diagnostic workup

- » **Urine drug test (UDS)**
- » **Gas chromatography-mass spectrometry (GC-MS)** by urine test is confirmatory
- » **CBC:** normal or anemia or ↑ WBCs
- » **BUN/Creatinine:** Normal or abnormal
- » **Serum electrolytes:** normal or deranged
- » **LFTs:** Normal or abnormal in infection
- » **Other test if indicated:** HbSAg, Anti-HCV, HIV, TB (PPD), RPR (syphilis), Blood culture

Induction therapy

- » Buprenorphine, Naloxone or naltrexone
- » Buprenorphine, ± Naloxone
- » Methadone

Rx

Prescription # 1

For pain management

(Neubrol forte, Provas-N)

1. **Tab. Paracetamol + Orphenadrine citrate**
OR **Tab. Paracetamol + Tramadol** (Tonoflex-p, Distalgesic)
I – I – I (TDS)

For CNS features:

2. **Tab. Lorazepam 1mg or 2mg** (Ativan, Tenzil)
OR **Tab. Alprazolam 0.5mg or 1mg** (Alp, Praz, Xanax)
OR **Tab. Clonazepam 0.5mg or 2mg** (Revotril, Naze)
OR **Tab. Estazolam 1mg or 2mg** (Esilgon)
0 – 0 – I (HS)
3. **Cap. Fluoxetine 20mg** (Prozac, Flux, Depex)
OR **Tab. Escitalopram 5mg or 10mg** (Estar, Citanew)
I – 0 – 0 (OD)

Flu-like syndrome

4. **Tab. Hydroxyzine 10mg or 25mg** (Atarax)
OR **Tab. Cetirizine 10mg** (Rigix, Zyretic)
I – 0 – I (BD)

For nausea/vomiting:

5. **Tab. Gravinate 50mg x TDS**
OR **Tab. Ondansetron 4mg x TDS**

Rx

Alternative Prescription # 2

For pain management

1. **Tab. Paracetamol + Orphenadrine** (Neubrol forte, Provas-N)
I – I – I (TDS)
2. **Tab. Tramadol 100mg** (Tramol SR, Tonoflex SR)
I – 0 – I (BD), I – I – I (TDS)

For CNS features

3. **Tab. Quetiapine 25mg or 100mg** (Qusel, Piquet, Evokalm)
Dosage: Initially 25mg than 50mg than 100mg x HS, titrated up to 300mg in BD/TDS doses. (Maximum 300-800mg/day)
4. **Tab. Olanzapine 5mg or 10mg** (Olanzia, Olepra, Nirvanol)
Dosage: Initially 2.5mg (½ of 5mg), titrated upto 10mg
½ – 0 – ½ x 3 days, Than ½ – 0 – I, than 5mg x BD

Flu-like syndrome

5. **Tab. Hydroxyzine 10mg or 25mg** (Atarax)
OR **Tab. Loratidine 10mg** (Softin, Lorin NSA)
I – 0 – I (BD)

For nausea/vomiting:

6. **Tab. Gravinate 50mg x TDS**
OR **Tab. Ondansetron 4mg x TDS**

CONVERSION DISORDER

Conversion disorder is also known as functional neurological symptom disorder. Patients present with neurological symptoms that cannot be fully explained by a neurological condition. Patients may be calm and unconcerned when describing their symptoms (sometimes referred to as "la belle indifférence").

Sex: Common in Female > Male, Age of onset: = 10 to 35 years of age.

Risk factors: History of sexual or physical abuse, childhood abuse, female sex (>75%), history of trauma related disorders, Emotional processing problems, recent psychological or physical stressors, remote life stressors, neuroticism (a tendency to experience negative emotions such as sadness, anxiety or mood swings)

CLINICAL FEATURES

- Patients may present with motor and/or sensory deficits affecting single or multiple areas of the body.
- Some clinical features are more commonly found in conversion disorder than in neurological conditions.

Functional paralysis	- Normal deep tendon reflexes - Paralysis does not follow anatomical patterns. Arm weakness: Drift without pronation, Positive finger abduction test Leg weakness: Positive Hoover sign, Positive hip abductor sign, Dragging gait
Psychogenic nonepileptic seizures	- Prolonged generalized seizure-like motor movements without loss of awareness During seizures: crying, side-to-side head shaking, clenching the eyes shut, hip thrusting, hyperventilation, eyes may be tightly closed and Tearfulness Tongue biting: more commonly on the tip of the tongue than the sides - Injuries, loss of bladder or bowel control, and postictal confusion are uncommon.
Functional dystonia	- Sudden and rapid progression. - Typically manifests with a clenched fist or an inverted foot/ankle. - Severe pain is common. - Symptoms do not improve with sleep. - Often has atypical triggers (e.g., a loud noise).
Functional tremors	- Sudden onset. - Varying location, frequency, amplitude, and/or direction. - Tremor reduces or changes with distraction. - Tremor worsens if weights are attached to the limb.
Functional visual disturbances	- Pupillary reflex present. - No signs of injury (e.g., bruises or scrapes) elsewhere on the body. - Visual acuity unchanged by reduction of distance from the eye chart. - Optokinetic drum elicits nystagmus.
Functional hearing loss	- Unable to direct gaze toward own hand or connect tips of own index fingers. - Patients blink in response to loud sounds.

Diagnostic approach

Diagnosing conversion disorder involves a thorough evaluation to rule out other medical conditions and to understand the psychological and contextual factors involved.

The process includes:

1. Clinical Assessment:

- Detailed medical history and physical examination
- Neurological examination to assess the symptoms

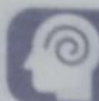
2. DSM-5 Diagnostic Criteria (according to DSM-5):

All of the following DSM-5 diagnostic criteria must be met:

- ≥ 1 neurological symptom (altered motor or sensory function): e.g., paralysis, muscle spasms, blindness, mutism, lump in throat, weakness, gait disorder

Clinical features:

- Are incompatible with any recognized neurological or medical condition
- Cannot be better explained by another medical disorder



- » Symptoms cause significant distress or psychosocial impairment or require medical evaluation
- 3. **Exclusion of other conditions:**
 - » Use of diagnostic tests (e.g., MRI, EEG) to rule out neurological disorders
 - » Assessment for other psychiatric disorders, such as somatic symptom disorder, factitious disorder, and malingering
- 4. **Psychological Evaluation:**
 - » Identify stressors, psychological conflicts, or trauma that may contribute to the symptoms
 - » Evaluate for comorbid psychiatric conditions (e.g., depression, anxiety)

TREATMENT OF CONVERSION DISORDER



The treatment of conversion disorder is multimodal and tailored to the individual, involving a combination of psychological, medical, and supportive interventions.

1. **Psychoeducation:**
 - » Explain the diagnosis and the mind-body connection in simple, non-technical language
 - » Reassure the patient that the symptoms are real and that recovery is possible
2. **Psychotherapy:**
 - » **Cognitive behavioral therapy (CBT):** Helps patients understand, change maladaptive thoughts and behaviors
 - » **Psychodynamic therapy:** Explores underlying emotional conflicts and stressors
 - » **Trauma-focused therapy:** For patients with a history of trauma, therapies such as Eye Movement Desensitization and Reprocessing (EMDR) can be effective
3. **Physical therapy:**
 - » Tailored exercise programs to improve mobility and function
 - » Techniques to reduce physical symptoms and improve physical capacity
4. **Occupational therapy:**
 - » Assist with activities of daily living
 - » Provide strategies to manage symptoms in everyday routines

Pharmacotherapy (Medication therapy): May be used to treat comorbid conditions such as depression or anxiety. Should be used cautiously and monitored for effectiveness

- » **Antidepressants therapy**
 - » Tab. Escitalopram 10mg or 20mg (Ciprexal, Estar, Citanew) x 10–20 mg PO once daily in the morning
 - » OR Cap. Fluoxetine 20mg (Flux, Prosac, Depex) starting at 20–80 mg PO once daily in the morning
- » **Anxiolytic (Benzodiazepines):** may be used until antidepressants take effect.
 - » Tab. Alprazolam 0.5mg OR 1mg (Alp, Praz, Xanax) at dose 0.5–2mg orally at night = 0–0–1 (HS)
 - » OR Tab. Clonazepam 0.5mg OR 2mg (Revotril, Naze) at dose 0.5–2mg orally at night = 0–0–1 (HS)

5. **Supportive interventions:**
 - » Involvement of family and caregivers in the treatment process
 - » Vocational rehabilitation to assist with return to work or school
 - » Social support to provide a network for the patient
6. **Regular follow-up:**
 - » Ongoing monitoring of symptoms and treatment progress
 - » Adjustment of treatment plans as necessary
 - » Strategies for relapse prevention and stress management
7. **Referral to specialists:**
 - » Neurologists, psychiatrists, or psychologists for specialized care
 - » Pain specialists if pain is a significant symptom
 - » Rehabilitation services for comprehensive functional rehabilitation





SCABIES

Scabies

C/C:

Incubation period: Approximately 3-6 weeks following infestation.

Intense pruritus that increases at night.

Burning sensation.

Skin lesions

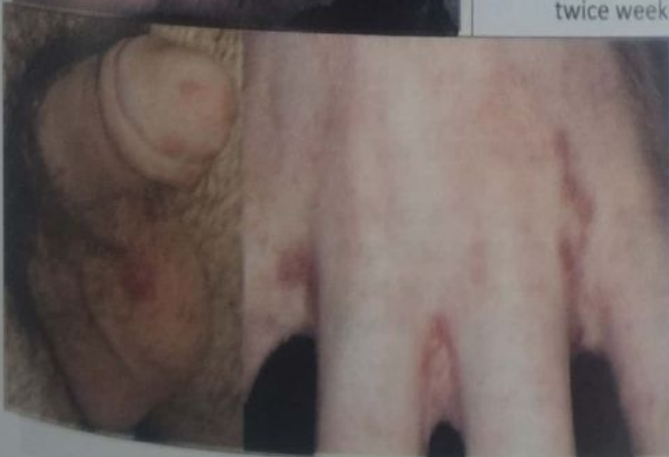
- Elongated, erythematous papules.
- Burrows of 2-10mm in length.
- Scattered vesicles filled with clear or cloudy fluid.
- Excoriations, pustules & secondary infection

Predilection sites

- Wrists (flexor surface)
- Medial aspect of fingers
- Interdigital folds (hands & feet)
- Male genitalia (scrotum, penis)
- All other intertriginous areas of the skin (anterior axillary fold, buttocks)
- Periumbilical area or waist
- **Additionally in children, elderly persons, & immunosuppressed patients:** scalp, face, neck, under the nail, palms of hands, and soles of feet

Alternative anti-scabies topical agents:

- Lindane (Lice-o-nil cream)
- Malathion topical
- Crothamiton (Scabion lotion/cream)
- Benzyl benzoate (SP lotion)



TREATMENT OF SCABIES

- Treat all household contacts whether symptomatic OR asymptomatic, can provide family members with prescriptions for treatment based on physician's comfort
- Wash all bed linens/clothing/towels with hot water and hot drying cycles

1. Permethrin 5% Cream OR Lotion (Lotrix, Scabfree, Mitonil)

- » Take a warm bath, dry the skin with separate towel and carefully apply a thin layer of permethrin 5% to the skin below collar line (face spared) from behind the ears down to the toes including creases and web spaces and leave on skin overnight. Wash off after 8-14 hours
- » May need to repeat treatment after 7 - 14 days if evidence of live mites.

2. Antihistamines: Tab. Loratidine 10mg (Softin, Lormax, Antial) OR Tab. Desloratadine 5mg (Destina, Desora, Neo-Antial) OR Tab. Levocetirizine 5mg (Belair, Xyzal, Neo-Sedil) OR Tab. Cetirizine 10mg (Rigix, Zyrtec) 1-0-1 (BD)

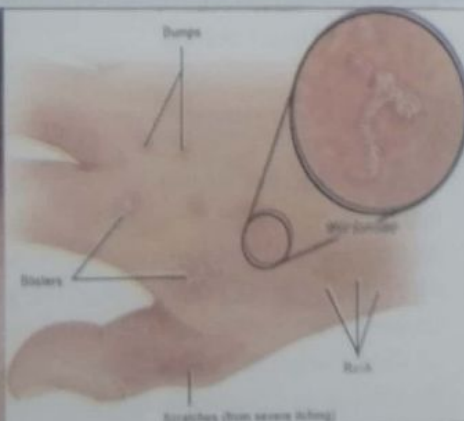
- **Post-scabetic pruritus:** Duration of pruritus can persist for up to 4 weeks post-treatment, continue Anti-histamine drugs. Topical steroids may be consider if indicated.

Tab. Ivermectin 6mg (Ivermite, Mectimite)

- **Indication:** Large outbreaks or severe form of scabies
- **Dosage:** 200 mcg/kg orally once daily on days 1, 2, 8, 9, and 15; additional doses may be required for severe cases on days 22 and 29.

Crusted (Norwegian) scabies (severe form of scabies)

- Combination therapy permethrin PLUS oral Ivermectin
- Apply permethrin from neck down to the soles of feet, wash off after 8-14 hours; repeat daily for 7 days and then twice weekly until cure.



ACNE VULGARIS

Clinical features	Risk factors
☛ Localization: Common in areas with sebaceous glands such as face, shoulders, upper chest, and back. ☛ Age of onset: typically, by 11–12 years, with symptoms usually disappearing around 20–30 years of age. ☛ Sex: more common in males during adolescence, but more common in female during young age. ☛ Non-inflammatory: comedonal acne » Closed comedones (whiteheads): closed small round lesions that contain whitish material (sebum and shed keratin). » Open comedones (blackheads): dark, open portion of sebaceous material. ☛ Inflammatory: affected areas are red and can be painful. » Papular/pustular acne: papules, pustules that arise from comedones. » Nodular acne (> 5 mm in diameter) ▪ Commonly affects the back and neck area. ▪ Severe form: Acne conglobata that is associated with cysts and abscesses.	» Genetic predisposition » Oil-based skin products/cosmetic products. » Hormonal imbalance » Infections: Bacterial colonization » Climate change, tobacco smoke, stress, insomnia » Drugs: anabolic steroids, corticosteroids, lithium, thyroid therapy, and progestin only pills. » Obesity, insulin resistance and PCOS » Congenital adrenal hyperplasia (CAH)
	Etiology
	1. Androgen stimulates sebaceous follicles to overproduce sebum → follicles become blocked. 2. In female due to menstrual cycle 3. Follicular Hyperkeratinization: Higher keratinocyte activity & ↓ keratinocyte shedding in pilosebaceous units leads to the formation of comedones. 4. Bacterial colonization with Propionibacterium acnes (Cutibacterium acnes).
General treatment and care	Guidelines for isotretinoin
☛ Provide general skin care instructions. » Use a gentle facial cleanser and avoid excessive cleaning and scrubbing (e.g., with exfoliants). » Avoid skin care products (e.g., moisturizers, cosmetics) that are comedogenic. » Do not pick at acne lesions. ☛ For individuals with endocrine-related acne (e.g., due to PCOS, obesity), advice exercise and weight loss for healthy BMI. ☛ Dietary restrictions & supplements with fish oil are not supported by current evidence. Duration of treatment: Following the initiation of an acne medication regimen, it typically takes 4–6 weeks to notice clinical improvement and at least 2–3 months to see clearing.	☛ 1 month prior to treatment for female who desire pregnancy: » Retinoid/Isotretinoin therapy should be discontinued at the latest one month before planned conception. » Perform the first of two serum and/or urine pregnancy tests to confirm the patient is not pregnant. » Provide counseling on contraception options and risk for birth defects. » Initiate two methods of contraception. ↳ '1' approved form of primary contraception ↳ '1' approved form of secondary barrier contraception » Repeat the pregnancy test after at least 30 days of using '2' approved forms of contraception, prior to starting isotretinoin. ☛ Laboratory monitoring for isotretinoin: 1. CBC: May show anemia. 2. Liver function test: ↑ AST, ↑ ALT 3. Fasting Lipid profile: ↑ Triglycerides, ↓ HDL 4. Blood sugar: ↑ Glucose.

Rx

TREATMENT OF MILD ACNE

1. **Acnes mentholatum face wash** OR **ACNE-AID liquid face wash** OR **Acure face wash** x Twice daily
2. **Adapalene gel** (Adapco, Clear) OR **Tretinoin cream** (Retin-A, Skin-A) OR **Isotretinoin gel** (Isotrex, Cosmin, Isotini) OR **Tazarotene 0.1%** (Tazene Gel, Tazret cream, Azoten cream) x Apply topically once daily at bedtime (HS) OR **Benzoyl peroxide + Clindamycin** (Duac gel, Benclin gel) x Apply topically once daily at bedtime (HS) OR **Benzoyl peroxide + Adapalene** (Acne-pearl plus gel, Adarex gel, Differin gel) x Apply once daily at bedtime (HS) OR **Clindamycin + Tretinoin** (Cleret gel, Acdermin gel) x Apply topically once daily at bedtime (HS) OR **Isotretinoin + Erythromycin** (Isotrexin gel, Clarixin gel, Erynocin gel) x once daily at bedtime (HS)

TREATMENT OF MODERATE ACNE

Rx

1. Acnes mentholatum face wash OR Acure face wash x Twice daily
2. Benzoyl peroxide + Clindamycin (Duac gel, Benclin gel) x Apply topically once daily at bedtime (HS).
3. Adapalene gel (Adapco, Clear) OR Tretinoin cream (Retin-A, Skin-A) OR Isotretinoin gel (Isotrex, Cosmin, Isotin) OR Tazarotene 0.1% (Trazene Gel, Tazret cream, Azoten cream) x Apply topically once daily at bedtime (HS).
4. If unresponsive/severe consider adding oral antibiotics: Tab. Minocycline 100mg (Minoderm, Minogen) x BD OR Cap. Doxycycline 100mg (Vibramycin, Doxyn) OR Tab. Doxycycline 100mg (Adoxa, Doxybact) x Twice daily (bd) on first day, then 100mg once daily (OD) for 6–12 weeks.
5. For itching: Tab. Loratidine 10mg (Softin, Lorin NSA) OR Tab. Levocetirizine 5mg (Belair, Xyzal, T-Day) x OD/BD

TREATMENT OF SEVERE (NODULAR/CONGLOBATA/RECALCITRANT) ACNE

Rx

1. Oral antibiotic (Minocycline, Doxycycline, Azithromycin) AND topical combination therapy as Moderate acne OR Cap. Isotretinoin 20mg (Arynoin, Isozam, Roaccutane) at dose of 0.3–0.5 mg/kg PO in 2 divided doses with food. Adult & children >12 years with severe recalcitrant acne: start isotretinoin at dose 0.5 mg/kg/day PO in 2 divided doses with food, titrate up after 1 month to 1 mg/kg/day PO for 2–3 months.
 - » Advise patients not to donate blood during treatment and for at least one month after treatment.
 - » Side effects: Teratogenicity, cheilitis, xerosis, conjunctivitis, pruritus, photosensitivity, & hypertriglyceridemia.
2. Consider adding Tab. Prednisolone 5mg (Deltacortril) at dose 5mg – 1mg once daily when starting isotretinoin.

TREATMENT GUIDELINES MANAGING ACNE VULGARIS

1. Mild type Acne: Few comedones inflammatory papules and/or pustules may be present.
 - » Topical benzoyl peroxide (comedolytic & bactericidal effects secondary to a release of oxygen free radicals)
 - » OR Topical Retinoids (Adapalene, Tretinoin, Isotretinoin, Tazarotene)
 - » OR Topical combination therapies
 - » Benzoyl peroxide AND Antibiotic (Clindamycin, Erythromycin) OR Retinoid (Adapalene, Tretinoin)
 - » Benzoyl peroxide AND Antibiotic (Clindamycin, Erythromycin) AND Retinoid (Adapalene, Tretinoin)
2. Moderate type Acne: Several comedones and inflammatory papules and pustules, Some nodules may be seen
 - » Combination topical therapy:
 - » Topical benzoyl peroxide AND topical retinoids (Adapalene) OR antibiotics (Clindamycin)
 - » Oral antibiotic may be added: Minocycline, Doxycycline, Azithromycin
 - » For female individuals of reproductive age: Add hormonal therapy such as Combined oral contraceptives pills (COCs): Tab. Ethinyl Estradiol 0.02mg + Drospirenone 3mg (Tab. Yaz) OR Tab. Cyproterone Acetate 2mg + Ethinylloestradiol 35mcg (Tab. Diane-35, Tab. Cyprodiol) x Once daily

Indications of COCs:

 - » Acne in patients seeking contraception
 - » Consider in female individuals of reproductive age with acne and: Symptoms of hyperandrogenism, Symptoms that worsen with menstruation, Limited response to other acne therapies.
3. Severe type Acne: Multiple comedones, inflammatory papules and pustules, nodulocystic acne may be present.
 - » Oral antibiotic (Minocycline, Doxycycline, Azithromycin) AND topical combination therapy as Moderate acne
 - » OR Oral isotretinoin therapy
 - » For female individuals of reproductive age: Add COCs – Tab. Yaz OR Tab. Diane-35 x once daily



SEBORRHEIC DERMATITIS (SEBORRHEIC ECZEMA)

Definition: Seborrheic dermatitis is a common inflammatory skin disorder that usually manifests as erythema and scaling of the scalp, nasolabial folds, glabella, and occasionally central face and anterior chest. It tends to worsen with stress. Infants may manifest as scaling of the scalp and is termed cradle cap.

ETIOLOGY

The etiology is unknown/unclear; may be associated with increased colonization of seborrheic areas by the commensal yeast (fungal infection) *malassezia furfur* species (formerly called *Pityrosporum ovale*).

Risk factors:

- » Oily skin (seborrhea – Oversecretion of sebaceous materials)
- » Neurological and psychiatric disease: Parkinson disease, stroke, Alzheimer dementia, major depression
- » Immuno-compromised state (HIV/AIDS), hormone problems, nutritional deficits, androgenetic alopecia
- » Familial history of seborrheic dermatitis, psoriasis.
- » Exposure to drug treatment: Dopamine antagonists, immunosuppressants, psoralen/PUVA, lithium

CLINICAL FEATURES

Symptoms

- » Most common: Burning, itching, scaling of the scalp (Scalp dandruff).
- » If severe, can become exfoliative erythroderma (as in those with immunodeficiencies)

On physical examination

- » Scaly, greasy, flaky skin on scalp margins and face
- » Ranges from erythematous plaques with patchy scaling → greasy yellow crusts, distributed along areas with hair and oily skin on the following sites:
 - ↳ Scalp scaling
 - ↳ Forehead/hairline and retroauricular area scaling
 - ↳ Nasolabial fold, eyebrows and periocular region (blepharitis: scaly red eyelid margins)
 - ↳ Glabella scaling
 - ↳ Presternal and interscapular regions
 - ↳ Axillae, under breasts, umbilicus, and groin area
- » White flakes: Greasy white flakes deposited on clothing and in hair.

Complication

- » Exacerbation of seborrheic dermatitis may lead to generalized erythroderma.
- » Secondary bacterial infection (Consider oral antibiotics if present).



TREATMENT OF SEBORRHEIC DERMATITIS (SEBORRHEIC ECZEMA)

1. General prevention

- » Frequent cleansing with soap removes oils from affected areas and improves seborrhea.
- » Patients should be counseled that good hygiene must be a lifelong commitment.
- » Exposure to the sunlight may help relieve symptoms.
- » Avoid precipitating factors if possible: Stress, cold and dry weather, sweating, harsh chemicals.

2. Apply Emollient (lotion, gel and spray-on oil forms) after washing.

3. Topical solution/shampoo for Scalp and beard: Initially application twice a week for a month, then once or twice a week for symptoms control. Massage into the scalp, then wait 5 minutes before rinsing then rinse hair and scalp well with warm water, and then dry the hair.

- » Pyrithione zinc 1% shampoo (Photonic shampoo, ZIKO shampoo, Zinsas shampoo)
 - » OR Coal tar 1% solution (Polytar scalp shampoo)
 - » OR Selenium sulphide 1% shampoo (Selsun blue)
 - » OR Ketoconazole 2% shampoo (Conaz, Nizoral, Ketwin)
 - » OR Medicated shampoo with Coal tar + salicylic acid (Photonic TAR, C-TAR)
 - » OR Medicated shampoo with Coal tar + Zinc Pyrithione (Megatar, Extar, Zintar plus)
- Apply to scalp 2-3 times weekly for 5 minutes then rinse scalp well with warm water

4. Additional treatment: Topical Potent steroids, if there is severe scalp itch
 - » Flucinolone acetonide 0.01% in olive oil topical solution (Flucinate, Derma-smooth)
 - » OR Desonide lotion 0.05% x Apply sparingly to the affected area(s) twice daily.
 - » OR Betamethasone 0.1% lotion (Betaderm, Betnovate, Betonil).
 - » OR Mometasone 0.1% lotion (Hivate, Santomet, Momate).
 - PLUS mix with liquid paraffin and coconut oil.
 - Apply sparingly to the affected area(s) twice daily for 1-2 weeks, then until inflammation clears (4 weeks).
5. For Face involvement: Low-potency topical steroids (Hydrocortisone 1%) for 1-2 weeks
6. Anti-histamine for itching: Tab. Levocetirizine 5mg (Belair, Xyzal) OR Tab. Cetirizine 10mg (Rigix, Zyretic) x BD
7. Consider systemic therapies for widespread or recalcitrant disease in adults
 - » Cap. Itraconazole 100mg (Icon, Sporanox, Rolac) at dose 200 mg/day x OD/BD for the first week of the month followed by 200 mg/day for the first 2 days for 2-11 months.
 - » OR Tab. Terbinafine 250 mg (Terbiderm, Terbisil) at dose 250 mg/day either as a continuous (4-6 weeks) or as an intermittent regimen (12 days per month) for 3 months.



PSORIASIS

Definition: Psoriasis is a common T-cell-mediated inflammatory skin conditions. The etiology is unknown, but is thought to be due to genetic inheritance and environmental triggers. Psoriasis typically manifests as sharply demarcated, erythematous, scaly, pruritic plaques, most commonly occurring on the scalp, presacral region, and extensor surfaces of the knees and elbows; however, any area of the skin may be affected.

ETIOLOGY

- » Genetic predisposition: Most likely determined via polygenic inheritance (PSORS1, HLA-B27 → psoriatic arthritis)
- » Trigger factors:
 - » Infectious: Infections of the upper respiratory tract (caused by beta-hemolytic streptococci), Staphylococcal infections, human immune deficiency virus (HIV)
 - » Medications: Beta-blockers, chloroquine, lithium, interferon alpha, TNF-alpha inhibitors, and NSAIDs
 - » Other causes: Trauma, cold weather, mechanical irritation, alcohol use, tobacco use, smoking, obesity, pregnancy and stress

CLINICAL FEATURES

- » Course: The disease course is relapsing, with symptom-free intervals
- » Cutaneous Lesions: Initially, a few single lesions typically appear, which then often become confluent.
 - » Well-demarcated, erythematous plaques, and/or papules with silvery-white scaling
 - » Mainly on scalp, back, elbows, and knees (extensor surfaces) but any site of the skin may be involved.
 - » Pruritus in 80% cases (typically mild, but may also be severe)
 - » Lesions characteristically show the Auspitz sign (Small pinpoint bleeding when scales are scraped off)
- » Cutaneous variants of psoriasis: (Classify by international counsel of psoriasis)
 1. Plaque psoriasis: most common variant (80-90% of cases); Raised inflamed plaque lesions with a superficial silvery-white scaly eruption. The scale may be scraped away to reveal inflamed & sometimes friable skin beneath.
 2. Guttate psoriasis: Widespread, erythematous, fine, scaly papules (water drop appearance) on trunk, arms, and legs. Occurs mainly in children and adolescents after upper respiratory streptococcal infection.
 3. Erythrodermic psoriasis: Generalized erythema with fine/diffuse scaling. It is often associated with pain, irritation, and sometimes severe itching. May lead to severe illness with fever and dehydration.
 4. Inverse psoriasis: mainly affects skin folds and flexural creases of large joints (flexural psoriasis)



5. **Pustular psoriasis:** High correlation with HLA-B27
- » **Acute generalized pustular psoriasis (rare, severe, urgent):** The most common subtype, characterised with Generalized erythroderma, confluent white pustules over the entire body, involvement of the oral mucosa and tongue. Relapsing course with pronounced malaise (fever, weakness, chills); may be fatal.
 - » **Palmoplantar pustulosis:** chronic involvement of hands and feet.

» **Involvement of nails (50% cases)**

- » **Nail pitting:** small, round depressions in the nail.
- » **Brittle nails:** nail dystrophy with crumbling of the nail.
- » **Onycholysis:** partial and mostly distal separation of the nail plate.
- » **Oil drop sign (or salmon spot):** well-circumscribed, yellow-reddish discoloration of the nail.

DIAGNOSTIC WORKUP

- » **Diagnosis:** Psoriasis is a clinical diagnosis based on patient and family history and thorough skin examination.
- » **Skin biopsy:** Consider only if clinical presentation is atypical. It is not routinely required for diagnostic confirmation.

MANAGEMENT GUIDELINES

1. **All patients**

- » **Assess disease severity:** e.g., based on estimated body surface area (BSA) affected.
 - » **Mild psoriasis** (below 3–5% BSA involvement on the basis of Wallace's rule of nines)
 - » Topical pharmacotherapy (e.g., corticosteroids, calcipotriene, retinoids) &/or targeted phototherapy
 - » Systemic agents if treatment response is insufficient.
 - » **Moderate to severe psoriasis** (above 3–5% BSA involvement on the basis of Wallace's rule of nines)
 - » Systemic pharmacotherapy and/or phototherapy
 - » Phototherapy: Narrowband UVB therapy/PUVA therapy
 - » Consider adjunctive topical pharmacotherapy.
- » **Provide supportive care:**
 - » Provide topical treatment with petroleum jelly and moisturizers to prevent moisture loss.
 - » Counsel on reducing alcohol use and smoking cessation.
 - » **Provide management of comorbidities:** The most common comorbidities associated with psoriasis are hyperlipidemia, hypertension, obesity, type 2 diabetes, and Mental health conditions (depression, anxiety).

2. **Topical pharmacotherapy:**

- » **Firstline is topical pharmacotherapy is the mainstay of mild psoriasis treatment for 4 weeks.**
 - » **Face, neck, or skin folds (i.e., areas with sensitive/thin skin):** Low-potency (Hydrocortisone 1%)
 - » **Scalp, trunk, and extremities:**
 - » **Medium-potency:** Triamcinolone 0.1%, Fluticasone 0.05%, Mometasone 0.05%
 - » **High-potency:** Betamethasone 0.05%, Clobetasol 0.05%, Fluocinonide 0.05%, Halobetasol 0.05%
- » **Topical calcineurin inhibitors (off-label use):** e.g., Tacrolimus 0.03 % or 0.1%, or Pimecrolimus 1%
 - » Alternative to steroids for areas with sensitive/thin skin.
 - » May be used for maintenance after > 4 weeks of steroid use.
- » **Additional therapy:** the following agents may be used in combination with topical corticosteroids.
 - » **Vitamin-D analogues:** e.g., Topical Calcipotriol/calcipotriene
 - » **Keratolytics:** Topical retinoids (e.g., Tazarotene), or Salicylic acid
 - » **Coal tar 1% lotion** (Polytar scalp shampoo)
- » **Commonly used combinations include topical corticosteroids plus either vitamin-D analogues or keratolytic agents. Combination therapy increases efficacy and may cause fewer adverse effects than monotherapy.**

3. **Systemic pharmacotherapy:**

- » **Principles of systemic therapy:**
 - » Management should be specialist/dermatologist guided.
 - » Before therapy initiation, obtain baseline laboratory tests: CBC, LFTs, Urea & creatinine, electrolytes.
 - » Adjunctive topical pharmacotherapy may be added after a careful review for possible interactions.
- » **Common indications:**
 - » Moderate to severe psoriasis.
 - » Mild psoriasis with insufficient response to topical agents.
- » **Treatment options**
 - » **Biologics:** IL-17 inhibitors (Brodalumab, Secukinumab), IL-23 inhibitors (Ustekinumab, Guselkumab), TNF- α inhibitors (Etanercept, Adalimumab, Infliximab).
 - » **Other drugs:** Methotrexate (+folic acid to reduce the adverse effects), Cyclosporine, Acitretin & Apremilast

TREATMENT MILD PSORIASIS

- Rx**
1. Steroids for areas with sensitive/thin skin (Face, neck, or skin folds – arounds genitals, between buttocks or breast):
 - » Hydrocortisone 1% cream (Hydrocortisone) x apply sparingly to the affected area(s) two to four times daily.
 2. Scalp, trunk, and extremities:
 - » Fluticasone 0.05% ointment/cream (Cutivate, Tioovate) x Apply to the affected side twice weekly.
 - » OR Betamethasone 0.05% ointment/cream (Clobivate, Dermovate, Clobederm) x apply sparingly to the affected area(s) once or twice daily for 2-4 weeks.
 - » OR Clobetasol 0.05% ointment/cream (Clobivate, Dermovate, Clobederm) x apply sparingly to the affected area(s) twice daily for a maximum of 2-4 weeks.
- One part (ایک حصہ) of steroids + max with Two part (دو حصے) of Petroleum jelly.
دوونو ملا کر صبح شام متاثرہ جگہ پر لگائیں
3. PLUS, Additional therapy 'below one' may be used in combination with topical corticosteroids:
 - » Calcipotriol 50mcg (Dervit, Daivonex) x Apply sparingly to the affected area(s) once or twice daily for 4 weeks.
 - » OR Tazarotene 0.1% (Tazret cream, Azoten cream, Trazene gel)
 4. Oral antihistamines for itching: Tab. Cetirizine 10mg (Rigix, Zyretic) Tab. Levocetirizine 5mg (Belair, Xyzal, T-Day) OR Tab. Loratidine 10mg (Softin, Lorin NSA) OR Tab. Desloratadine 5mg (Destina, Desora, Neo-Antial) x OD/BD
- Combination therapies: Calcipotriol + Betamethasone (Dervit-B, Calcibet, Daivobet), Halobetasol/tazarotene (Duobrii)

TREATMENT MODERATE TO SEVERE PSORIASIS

- Rx**
1. Management should be specialist/dermatologist guided.
 2. The treatment is based on disease severity, the presence of comorbid conditions, and pregnancy.
 3. Initial treatment with Phototherapy (narrow-band UVB or PUVA therapy).
 4. Before initiating systemic therapy, obtain baseline laboratory investigations: CBC, LFTs, BUN, creatinine, electrolytes, fasting lipid profile, Fasting blood glucose, Tuberculosis (TB) screen, vitamin-D level, pregnancy test and Chest X-ray.
 5. SPECIALIST GUIDED SYSTEMIC PHARMACOTHERAPY:
 - » Tab. Methotrexate 2.5mg (Unitrexate) at dose 7.5-25 mg once weekly on the same day of each week. Should not exceed 30mg/week. Folic acid (5mg/day except the day of methotrexate) can be taken daily while receiving methotrexate. Careful review for possible interactions (e.g., PPIs, salicylates, NSAIDs, phenylbutazone, Phenytoin, sulfonamides, probenecid, cisplatin, mercaptopurine, oral antibiotics, other potential hepatotoxins, theophylline)
 - » OR Tab. Cyclosporine modified at dose 2.5 to 4 mg/kg/day orally given in 2 divided doses.
 - » OR Tab. Acitretin 25mg (Acetin, Neotret) at dose 25-50 mg orally once daily
 - » OR Tab. Apremilast 30mg (Apremist) at dose 10 mg orally once daily, in the morning on day 1, followed by 10 mg in the morning and 10 mg in the evening on day 2, then 10 mg in the morning and 20 mg in the evening on day 3, then 20 mg in the morning and 20 mg in the evening on day 4, then 20 mg in the morning and 30 mg in the evening on day 5, then 30 mg twice daily thereafter.
 - » OR Inj. Etanercept 50mg (Enbrel, Momentum) at dose 50 mg subcutaneously twice weekly for 3 months, followed by either 50 mg once weekly or 25 mg twice weekly, each dose should be 3-4 days apart.
 - » OR Inj. Adalimumab 40mg/0.4ml (Humira) at dose 80 mg subcutaneously on day 1, followed by 40 mg every other week starting 1 week after initial dose.
 - » OR Inj. Infliximab 100mg/vial (Remicade) at dose 5 mg/kg I.V at weeks 0, 2, 6, and then every 8 weeks thereafter.
 - » OR Inj. Secukinumab 150mg/ml (Cosyntax) at dose 300 mg subcutaneously at weeks 0, 1, 2, 3, and 4, followed by 300 mg every 4 weeks thereafter.
 6. Adjunctive topical pharmacotherapy may be added after a careful review for possible interactions (see above – mild)



TINEA CAPITIS

△ Tinea Capitis

C/C:

- » **Definition:** dermatophyte infection affecting the head and scalp, Tinea capitis is also known as ringworm and herpes tonsurans infection
- » **Epidemiology:** Affects children mainly > Adults
- » **Pathogen:** Trichophyton tonsurans (most common), Microsporum canis, Microsporum audouinii
- » **Location:** On the scalp ("capitis" = "head")
- » **Predisposing factors**
 - » Contact with infected individuals or animals
 - » Shared combs and hats
 - » Athletes with head-to-head contact (wrestling)

» Clinical Presentation

Symptoms:

- » Round, pruritic/itchy scaly plaques with broken hair shafts or hair loss in affected areas.
- » May mimic seborrheic dermatitis

Physical exam

- » Single or multiple scaly patches on the scalp
- » Alopecia with small black dots from broken-off hairs
- » Cervical/Postauricular lymphadenopathy
- » **Less common**
 1. **Kerion:** Severe form of tinea capitis characterized by a deep, inflammatory, boggy plaque with drainage and crusting (pustule formation)
 2. **Favus:** Perifollicular erythema progresses to yellow cupping

» Diagnostic Workup: KOH, Fungal culture

» Prognosis: Excellent since most cases resolve with treatment

Rx

General prevention

- » Avoid sharing personal items such as hats, hairbrushes, combs, pillows and helmets.
- » Keep your child's scalp clean and dry.
- » Keep children infected with tinea capitis away from healthy children.
- » Avoid places where your child can pick up the infection.
- » **Management of close contacts**
 - ↳ **Indication:** when multiple children are in the home
 - ↳ **Treatments:** use of antifungal shampoo by all house members, avoid sharing and clean hair clippers, combs, and hats

1. **Tab. Terbinafine 250mg** (Lamisil, Terbiderm, Terbisil) at dose 250mg orally once daily for 4 – 6 weeks
OR **Tab. Griseofulvin 500mg** (Graso-F, Grifin) at dose 500-1000 mg per day orally given in 1 to 4 divided doses for 4 to 6 weeks.
OR **Cap. Itraconazole 100mg** (Icon, Sporanox, Rolac) at dose 100 – 200mg once or twice daily for 4-6 weeks
2. **Adjunct: Topical antifungal shampoo**
 - ↳ **Selenium sulfide topical** (Selsun blue shampoo) Apply to scalp twice weekly for 4 weeks, leave each application on scalp for 3 minutes then rinse.
 - ↳ OR **Ketoconazole shampoo** (Conaz, Ketowin, Nizoral) Apply to scalp 2-3 times weekly for 2-4 weeks, leave each application on scalp for 5 minutes then rinse.
3. **Oral anti-histamine for itching/pruritis**
 - ↳ **Tab. Loratidine 10mg** (Softin, Lorin NSA)
 - OR **Tab. Cetirizine 10mg** (Rigix, Zyretic)
 - OR **Tab. Levocetirizine 5mg** (T-day, Belair, Xyzal)
 - One tablet once or twice daily



TINEA PEDIS (ATHLETE'S FOOT) & TINEA MANUUM

Most commonly caused by microsporum & trichophyton. Dermatophyte infection of the foot (Tinea pedis) & hand (Tinea manuum)

Predisposing factors

- » Closed, tight footwear
- » Public showers

Clinical features

Interdigital (most common): chronic, pruritic, erythematous scaling and erosions between the toes/fingers

Moccasin: hyperkeratotic thickening of the skin on soles of feet

Vesicular: pruritic or painful vesicular lesions and erythema, often on the medial foot

Diagnostic Workup

- » KOH
- » Fungal culture
- » Bacterial culture

Rx

General Prevention

- » Keep feet clean, dry, and cool.
- » Avoid using swimming pools, public showers, or foot baths.
- » Wear sandals when possible or air shoes out by alternating them every 2-3 days.
- » Avoid wearing closed shoes and wearing socks made from fabric that doesn't dry easily (for example, nylon).

1. **Topical Miconazole cream** (Daktarin) x apply topically BD

OR **Clotrimazole cream** (Canesten) x apply topically BD

OR **Terbinafine Cream** (Terbiderm, Terbisil) x apply BD

2. **For itching:** Tab. **Levocetirizine 5mg** (Belair, Xyzal) x OD/BD

OR Tab. **Cetirizine 10mg** (Rigix, Zyretic) x OD/BD

For more extensive disease or not respond to topical therapy

3. Tab. **Terbinafine 250mg** (Terbiderm, Terbisil) OD for 2 weeks

OR Cap. **Fluconazole 50mg** (Fungone) OD for 2-4 weeks.

OR Cap. **Itraconazole 100mg** (Icon, Rolac, Sporanox) x Once daily for 15 days OR 200 mg daily for 7 days.



TINEA CRURIS (JOCK ITCH)

Fungal infection of the inguinal area

Pathogen: most common tinea rubrum

Clinical presentation

- » Pruritic erythematous plaque that grows centrifugally
- » Similar to tinea corporis but often without central clearing
- » Scaling, raised border
- » Sparing the scrotum

Rx

Prevention

- » Stay dry, Keep your groin area dry
- » Wear clean clothes. Change your underwear at least once a day or more often if you sweat a lot.
- » Find the correct fit.
- » Don't share personal items.

1. **Ketoconazole Cream** (Nizoral, Conaz)

OR **Terbinafine Cream** (Lamisil, Terbiderm, Terbisil)

» Apply topically twice daily on affected site at least for 2 weeks

2. **For itching/pruritis:** Tab. **Cetirizine 10mg** (Rigix, Zyretic) x OD/BD

OR Tab. **Levocetirizine 5mg** (T-day, Belair, Xyzal) x OD/BD

For more extensive disease or not respond to topical therapy

3. Tab. **Terbinafine 250mg** (Terbiderm, Terbisil) x OD for 2-6 weeks

OR Cap. **Itraconazole 100mg** (Icon, Sporanox) at dose 100-200 mg/day (Max 400mg/day) for 2-4 weeks x OD/BD



TINEA CORPORIS (BODY RING WORM)

△ Tinea corporis (Body ring worm)
C/C:

Predisposing factors: Previous tinea infection, Contact with infected individuals or animals, Moist environments (e.g., public swimming pools), immune deficiency, Diabetes

CLINICAL FEATURES

- » Initially ring/round-shape, pruritic, erythematous plaque that grows centrifugally. **Itch is common.**
- » Develops into round, pruritic/itchy plaque with central clearing and a scaling, raised border
- » **Clinical variants of tinea corporis:** Kerion, Tinea gladiatorum, Tinea imbricata, Tinea incognito and Majocchi granuloma.

DIAGNOSTIC WORKUP

- » Obtain KOH
- » Obtain fungal culture

N.B. We do not recommend oral ketoconazole due to risk of severe liver injury and adrenal insufficiency.



Rx

General prevention

- ↳ Don't share clothes, sports gear, or towels.
- ↳ To wear slippers in locker rooms & public pool & bathing areas.
- ↳ To shower after any sport that includes skin-to-skin contact.
- ↳ To wear loose-fitting cotton clothes.
- ↳ To keep skin clean and dry.
- ↳ To take the pets to the veterinary if it has patches of missing hair, which could be a sign of a fungal infection.

1. Topical antifungal:

- ↳ **Terbinafine cream** (Terbiderm, Terbisil, Lamisil)
Apply topically to the affected area(s) twice daily for 1-3 weeks
- OR **Miconazole 2% cream** (Daktarin, Macnaz)
Apply to the affected area(s) twice daily for 2-4 weeks
- OR **Ketoconazole cream** (Nizoral, Conaz)
Apply to the affected area(s) once daily for 2-6 weeks

↳ **Adjunct: Aluminum acetate topical**

Topically applied on the skin as an antiseptic solution, twice daily for 15-30 minutes for 7 days to reduce itching, burning, and inflammation from skin irritations

2. Anti-histamine for itching/pruritis

- ↳ **Tab. Cetirizine 10mg** (Rigix, Zyretic)
- OR **Tab. Levocetirizine 5mg** (T-day, Belair, Xyzal)
- OR **Tab. Loratidine 10mg** (Softin, Lorin NSA)
- Orally once or twice daily

For more extensive disease or not respond to topical therapy**3. Tab. Terbinafine 250mg** (Lamisil, Terbiderm, Terbisil)

One tablet orally once daily for 2 – 6 weeks

OR **Cap. Itraconazole 100mg** (Icon, Sporanox, Rolac)

Dosage: 100–200 mg/day (Max 400mg/day) for 2 – 4 weeks x OD/BD

OR **Cap. Fluconazole 150mg** (Fonaz, Fungone, Diflucan)

One capsule of 150 mg orally once weekly for 2 – 4 weeks.



TINEA VARSICOLOR (PITYRIASIS VARSICOLOR)

Definition: Pityriasis versicolor is a superficial fungal infection of the stratum corneum, caused by due to dimorphic yeasts of the genus **Malassezia** (Normal flora, Becomes pathogenic when the yeast phase converts to mycelial phase), leading to hypo- or hyperpigmented macular lesions on seborrheic areas of the trunk.

△ Tinea versicolor

C/C:

Risk factors

- » High temperature, hot humid climates when the disease may be very extensive.
- » Excessive sweating, seborrhea & oily skin
- » Use of oily or greasy skin care products.
- » Cushing syndrome, malnutrititions and OCPs use
- » Systemic corticosteroids & Immunosuppression
- » Genetic predisposition, oily greasy skin
- » Athletes due to excessive sweating.

Clinical features: Round, well-demarcated macules that reveal a fine, subtle scale with gentle scraping that can coalesce into patches (which may have irregular shapes)

» Colors vary

- **Pityriasis versicolor alba:** pale patches (hypopigmentation)
- **Pityriasis versicolor rubra:** reddish-brown (hyperpigmentation)
- » Lesions do not tan in the sunlight, because of which they are more commonly noticed in the summer.
- » Milder pruritus (compared to dermatophyte infections)
- » Common sites are the trunk and chest, but the neck, abdomen, upper arms, and thighs may also be affected.

Diagnostic Workup:

- » **Potassium hydroxide (KOH) microscopy:** short hyphae and budding yeast with spaghetti-and-meatballs appearance
- » **Wood's light examination:** will fluoresce yellow/green
- » **Other test:** Skin biopsy, culture, gram stain

Rx

Prevention and prognosis:

- » Because the rash occurs more readily in hot, humid conditions, keep your skin as dry and cool as possible when you are in this climate.
- » The lesions will resolve without any permanent changes within 1–2 months of therapy.
- » Recurrences are common and treatment may need to be repeated intermittently.

1. Selenium sulfide topical (Selsun blue shampoo)

- » Apply to whole neck, trunk, arms, and legs once daily for 1 week then once weekly and leave for 2 to 3 minute than rinse thoroughly

OR Pyrithione zinc topical: apply to whole neck, trunk, arms, and legs once daily for 2 weeks

OR Propylene glycol topical: apply to whole neck, trunk, arms, and legs twice daily for 2 weeks

2. Ketoconazole Cream (Conaz, Nizoral)

OR Terbinafine solution OR cream (Terbiderm, Terbisil)
Apply topically twice daily for 2–4 weeks

3. Cap. Itraconazole 100mg (Sporanox, Icon)

Two time daily for one week with reevaluation 4 weeks
400 mg orally once daily for 3 days, OR 200 mg orally once daily for 7 days

OR Cap. Fluconazole 150mg (Fonaz, Fungone, Diflucan)

Dosage: 300 mg once weekly for 2 weeks (safest, most evidence) OR 400 mg orally as a single dose

Prophylaxis

- » **Cap. Itraconazole 100mg (Icon, Sporanox, Rolac)**
Dosage: 400mg once monthly for 6 months



ONYCHOMYCOSIS (TINEA UNGUIUM/FUNGAL NAIL)

- Definition: Superficial fungal infection of the nail (tinea unguium), involving nail bed and underside of nail plate.
- Pathogen: Dermatophytes (most commonly *T. rubrum* (referred to as *T. unguium*))
- Risk factors: Moist & warm environment, increasing age, immunosuppression, occlusive shoes, communal baths

Clinical features

- Symptoms: asymptomatic
- Location: Toenails > fingernails
- Physical exam
 - Distal and lateral or proximal subungual onychomycosis
 - Thickened with white, yellow, or brown discoloration & brittle nails.
 - Thickened nail may separate from nail bed (onycholysis)
 - Most commonly affects 1st or 5th nail.
 - Superficial white onychomycosis
 - White discoloration of nail plate
 - Powder-like

Diagnostic workup

- Potassium hydroxide (KOH) microscopy
- Fungal culture
- Bacterial culture

General Prevention

- Keep hands & feet clean, dry, and cool.
- Keep fingernails and toenails short and clean.
- Don't walk barefoot in areas like locker rooms or public showers.
- Don't share nail clippers with other people.
- Wear sandals when possible or air shoes out by alternating them every 2-3 days.
- wearing absorbent socks
- When visiting a nail salon, choose a salon that is clean and licensed by your state's cosmetology board. Make sure the salon sterilizes its instruments (nail clippers, scissors, etc.) after each use, or bring your own.

Rx

- Advise General prevention
- First line – systemic terbinafine therapy:
 - Tab. Terbinafine 250mg (Terbiderm, Terbisil)
 - For fingernails onychomycosis at dose 250mg once daily for 6 weeks.
 - For toenails onychomycosis at dose 250mg once daily for 12 weeks.

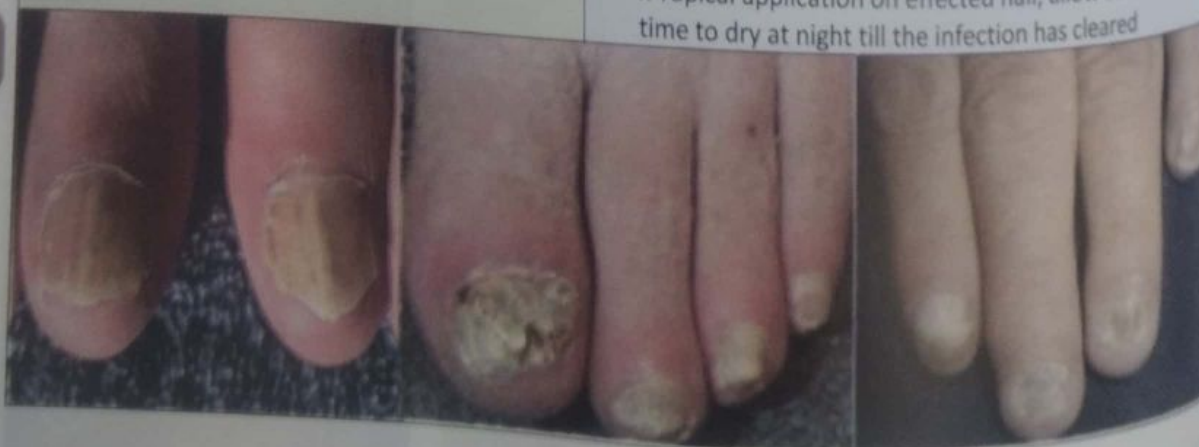
Second-line systemic AZOLE

- Cap. Itraconazole 100mg (Icon, Sporanox, Rolic)
 - Fingernails onychomycosis at dose 200 mg orally twice daily for 7 days, followed by no treatment for 21 days, then 200 mg twice daily for 7 days
 - For toenails onychomycosis at dose 200mg once daily for 12 consecutive weeks.
- OR Cap. Fluconazole 150mg (Fungone, Diflucan) at dose 150-450 mg orally once weekly for 6-12 months (toenails) or 3-6 months (fingernails).

Indication of topical antifungal → When there is < 80% nail involvement and No involvement of the lunula.

- Ciclopirox 8% topical application to affected nail(s) once daily, remove with acetone every 7 days and repeat application cycle.
- OR Efinaconazole 10% topical application to the affected nail(s) once daily for 48 weeks
- OR Tavaborole 5% topical application to the affected nail(s) once daily for 48 weeks.

- Supportive solution for Onychomycosis: Onychonil nail paint OR Onsis nail paint OR Lacqueryl nail lotion
x Topical application on effected nail, allow sufficient time to dry at night till the infection has cleared



PITYRIASIS ROSEA

Definition: Pityriasis rosea is a self-limiting rash, lesions usually resolve over 2 to 12 weeks, most commonly affects female > male, aged 10 - 35 years. The majority of patients present with a solitary, coin-sized herald patch, followed by multiple, oval, scaly papules distributed in a classic Christmas tree pattern (fir-tree pattern) on the trunk.

ETIOLOGY

The exact etiology is unknown (Idiopathic), pityriasis rosea is thought to be triggered by viral infection.

May be due to HHV-6 & HHV-7 is suspected based on the following:

- » Pityriasis rosea can occur in clusters, affecting many people living in the same community.
- » Seasonal variations (more common in the spring and fall).
- » Preceded by a prodromal flu-like illness in some patients.
- » Life-long immunity (recurrence is rare but possible).

CLINICAL FEATURES

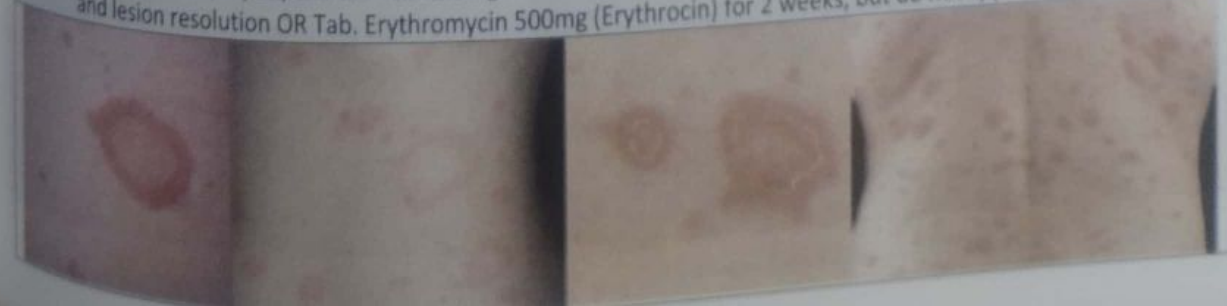
- » **Prodrome (1-2 weeks prior to rash onset):** Flu-like symptoms (e.g., malaise, fever, pharyngitis)
- » **Initial eruption (= 90% of cases):** Herald patch (mother patch), Typically, on the back
 - » Single ovoid macule or patch, 2-10 cm in diameter
 - » Slightly raised, dark red border with a central salmon-colored clearing zone
 - » **Surrounded by a collarette:** a collar of fine, white scales (like cigarette paper)
- » **Secondary eruption (2-21 days later)**
 - » Bilateral diffuse, oval-shaped, salmon-colored papules and plaques (< 1.5 cm) with scaly collarette
 - » Papules appear along Langer lines, which align on the back like the branches of a Christmas tree "appearance".
 - » **Typically seen on the trunk** (thorax, back, abdomen), neck, and upper extremities
- » **Pruritus:** moderate to severe itching in 50% of cases; absent in 25%.
- » **Post-inflammatory hypopigmentation or hyperpigmentation** (resolves over several months)

Diagnostic workup

- » Usually a clinical diagnosis
- » Laboratory tests may be considered if the diagnosis is uncertain.
 - » Potassium hydroxide (KOH) preparation: to exclude fungal infection (tinea).
 - » RPR or VDRL (to exclude secondary syphilis): Negative.
- » Skin biopsy: if the rash does not resolve after 3-4 months, the presentation is atypical, or the diagnosis is uncertain.

TREATMENT OF PITYRIASIS ROSEA

- » Watchful waiting, most cases are self-limited and require no treatment, Spontaneous resolution within 6-8 weeks
- » Provide reassurance to the patient. (Ref: aafp, NIH, Merck manuals guidelines)
- » **Mild to moderate cases**
 - » Avoid irritants (harsh soaps or fragrances, sweating, scratching)
 - » **Topical emollients (may diminish the appearance of scale):** Preparation of Zinc oxide lotion/calamine lotion (or menthol-phenol, pramoxine, or oatmeal)
 - » **Oral antihistamines for itching:** Tab. Cetirizine 10mg (Rigix, Zyrtec) OR Tab. Loratidine 10mg (Softin, Lorin-NSA) OR Tab. Levocetirizine 5mg (T-Day, Xyzal) OR Tab. Fexofenadine 180mg (Fexo, Telfast) x Once daily.
 - » **Adjunct:** Hydrocortisone 1% cream x Apply sparingly to the affected area's twice daily for 2 weeks
- » **Severe cases (severe pruritus or widespread rash)**
 - » **Clobetasol 0.05% cream** (Clobevate, Dermovate) x Apply Twice daily ± Short course of Tab. prednisolone 5mg (Deltacortril) 20 mg/day for 5 days, 15 mg/day for the next 5 days, and 10 mg/day for the last 5 days.
 - » UVB phototherapy (narrowband ultraviolet B therapy) in resistant cases 2-3 times/week until resolution
 - » Tab. Acyclovir (Acylex) at dose 400-800mg x 5 times/day for 7 days, had significant improvements in symptoms and lesion resolution OR Tab. Erythromycin 500mg (Erythrocin) for 2 weeks, but do not appear to be beneficial.



MELASMA

- ☞ **Definition:** Also known as chloasma, a benign disorder characterized by hyperpigmentation of the skin that is associated with pregnancy and oral contraceptive use.
- ☞ **Epidemiology:** More commonly in women (Female > male) of darker skin tones
- ☞ **Etiology:**
- » Unknown, exacerbated by sun exposure.
 - » **Pregnancy:** referred to as "mask of pregnancy"
 - » Hormonal contraceptives
 - » Neoplastic diseases that produce hormones, often associated with high levels of estrogen

△ Melasma

C/C:

- » Symmetric macular (flat) eruption of brown hyperpigmentation, typically well-defined borders
- » Common in the forehead, upper lip, chin, malar eminences, and neck
- » Non-erythematous, non-inflammatory
- » Exacerbated by exposure to sunlight (UV radiation)

Diagnosis: clinical diagnosis based on history, exam

What Not To Miss

- » Exogenous hyperestrogenism including OCPs, hormone replacement therapy
- » Role of visible light
- » **Exogenous ochronosis**
 - Look for stippled blue appearance

Differential diagnosis:

- » Post-inflammatory hyperpigmentation
- » Riehl's melanosis
- » Atypical periorbital acanthosis nigricans
- » Drug related hyperpigmentation (HCTZ, CCBs)
- » Lentigines

Work Up

- » Look for typical acanthosis nigricans at other sites if considering periorbital acanthosis nigricans
- » Post-pregnancy, melasma may fade in lighter skin types but persist in skin of color

Rx

☞ **Sun avoidance (Photo-protection) & Sunscreen use**

- » Broad-brimmed hats, sunglasses, photoprotective clothing
- » **Sunscreen with SPF 30 to 50+**

☞ **Cessation of contraceptives**

1. **Skin aqua clear white SPF 50+** (by Atco)
OR **Ultra sheer SPF 50+** (by Neutrogena)
OR **Photoderm spot SPF 50+** (by Bioderma)
OR **Solar max SPF 50+**

Twice daily (صبح، دوپہر کو چہرے پر لگائے)

2. **Revoderm Cream**

OR **Maxdif Cream**

OR **Lumexa Cream**

OR **Triderm Cream**

OR **Prosil gel**

Apply at face in night time (رات کو چہرے پر لگائے)

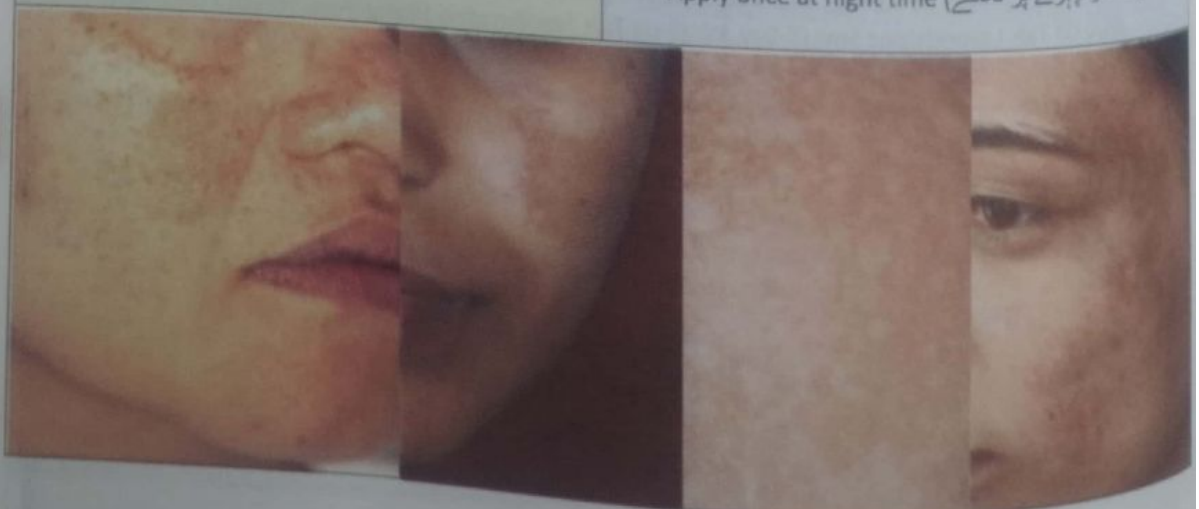
If not responding than consider

- ☞ **Topical depigmenting agents:** hydroquinone in combination with tretinoin and a mild corticosteroid to prevent irritation.

(Hyderquin plus, Lazma, Tri-melasin)

Hydroquinone + Fluocinolone + Tretinoin cream

Apply once at night time (رات کو چہرے پر لگائے)



VITILIGO

- Vitiligo is a common skin condition in which a patchy loss of epidermal melanocytes results in depigmentation.
- This loss is hypothesized to be a result of autoimmune destruction, oxidative stress, and/or intrinsic melanocyte defects in genetically predisposed individuals, and is commonly associated with other autoimmune diseases.
- The clinical course is highly variable, with unilateral or bilateral distribution of well-demarcated, depigmented macules, which may progress during the course of the disease.
- These lesions have a predilection for facial, acral, extensor, and sun-exposed areas of the body. Vitiligo is often a clinical diagnosis, but Wood lamp examination, dermoscopy, and/or skin biopsy are useful in ambiguous cases.

Classification according to location

Generalized (most common): widespread distribution of lesions, frequently with mucosal involvement 1. Acrofacial: lesions mainly on the hands and face 2. Vulgaris: patches that are widely distributed 3. Mixed: a combination of segmental and non-segmental vitiligo 4. Universal: almost the entire body affected	Localized: isolated area affected (e.g., dermatomal) 1. Focal: one or more lesion in one area (commonly trigeminal nerve distribution) 2. Segmental: unilateral, asymmetric lesions that follow dermatomal patterns; a common variant in children 3. Mucosal: only the oral and genital mucosa affected.
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Classification according to clinical course and prognosis

Segmental: - It is also called unilateral vitiligo, happens on one part of the body. - early onset, rapidly spreading; depigmented lesions may remain unchanged for life - It often starts at a young age and usually stops spreading after a year.	Non-segmental: - It is also called bilateral or generalized vitiligo - It may appear on all body parts, especially areas that are bumped or rubbed frequently. - These patches often extend slowly over time if left untreated. - A family history and progression of disease are common.
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△ Vitiligo C/C:

- Irregular, well-demarcated, depigmented (white) macules or patches, surrounded by normal skin.
- Unilateral or bilateral distribution, with stable or slowly progressive lesions.
- Commonly on the face (e.g., perioral and periocular regions), neck, scalp, acral surfaces (e.g., hands), extensor surfaces, or genitalia.
- Leukotrichia:** depigmented hair; an indicator of poor prognosis.
- Coexisting Autoimmune Diseases** (=20% of patients)
 - Most Common:** Hashimoto thyroiditis and Graves' disease
 - Other disorders:** Type 1 diabetes, psoriasis, Inflammatory bowel disease, Alopecia areata, Pernicious anemia, Addison disease
- Depigmentation of the retina may also occur.



Limited disease prescription #1

General measures

- Sunscreen (to Prevent Burns):** Always apply a sunscreen, ideally with a sun protection factor (SPF) of 30 or above, to protect your skin from sunburn and long-term damage.
- Temporary makeup to color skin
- Skin camouflage creams:** it can be applied to the white patches of skin. The creams are made to match your natural skin colour. The cream helps to blend the white patches with the rest of your skin, so they are not as noticeable.
- Oral antioxidant and Vitamin-D supplementation
- Topical corticosteroids** (If <10% body area are involved)
 - Betamethasone cream or ointment** (Betnovate, Prostate)
 - OR Fluticasone cream or ointment** (Cutivate, Ticovate)
 - OR Mometasone cream** (Hivate, Santomet)
 - Topical application twice daily on affected site x Every 2 weeks for 4-6 months. (On sensitive areas like face, neck or groin it should be used once daily).
- Topical Calcineurin Inhibitors** are alternative to topical corticosteroids and to minimize the risk of skin atrophy due to steroid use. For spots on an adult's face, eyelids, genitals, breasts or underarms a less irritating ointment tacrolimus 0.1% is preferable
 - Tacrolimus 0.1% Ointment** (Crolimus, Eczemus)
 - Topical application twice daily on affected site

Diagnostics

- » Usually a clinical diagnosis
- » If diagnosis is uncertain:
 - **Wood lamp examination:** The vitiligo lesions appear as well-defined blue-white areas.
 - **Dermoscopy:** Vitiligo lesions have a characteristic perilesional hyperpigmentation & telangiectasia.
 - **Skin biopsy and histology:** Melanocytes are absent, perilesional lymphocytes may be seen
- » **Serological markers of autoimmune disease:** Thyroid function tests and antithyroid antibodies once vitiligo is confirmed

Follow-up: After 1 month

Surgical Options include

- » Split-skin grafts
- » Mini/punch graft

Surgical procedures aim to replace the melanocytes with ones from a normally pigmented autologous donor site. Several melanocyte transplantation techniques can be performed under local anaesthesia in an outpatient facility. However, transplantation for extensive areas may require general anaesthesia. All methods require strict sterile conditions.



Rx

Limited disease prescription #2

- » If a patient does not respond to the previous option, then high-potency topical corticosteroids
- » A pulse treatment with 0.1% clobetasol, alternating with 0.1% tacrolimus ointment in a one week on/one week off regimen is often reported to provide good repigmentation.
- » **Clobetasol Cream or ointment** (Clobivate, Dermovate, Clobetol) Topical application twice daily on affected site x for 6-8 months (On sensitive areas like face, neck or groin it should be used once daily).
- » **Tacrolimus 0.1% Ointment** (Crolimus, Eczemus) Topical application twice daily on affected site
- » Consider Oral corticosteroids if not respond (Mention below)

For Progressive or refractory disease

Second line therapy: Primarily focus on improving skin appearance with a combination of topical, systemic and UVB phototherapy treatments. Such treatment duration varies from 8 to 24 months of two- to thrice-weekly treatments, with an average 65-75% success rate.

Phototherapy» **Narrowband ultraviolet-B (NB-UVB) phototherapy**

- It is the treatment of choice for non-segmental, generalized vitiligo.
- NB-UVB produces better repigmentation than PUVA, with better color match and fewer side effects.
- NB-UVB therapy is also better tolerated, and could be used on expecting or nursing women, and children.
- Combination interventions are superior to monotherapies like NB-UVB with 0.1% tacrolimus ointment.
- » Psoralen with ultraviolet-A phototherapy
- » PUVA phototherapy

If a patient has rapidly expanding vitiligo, with new spots appearing every week or existing ones getting bigger, then advice

» **Oral Corticosteroids**

- » **Tab. Prednisolone 5mg** (Deltacortril, Rapicort)
OR **Tab. Betamethasone 0.5mg** (Betnelan, Betnesol)
Two days a week for 16 weeks

» **Immunosuppressants drugs:**

- » **Tab. Azathioprine 50mg** (Imuron, Amorin) x half tablet daily
Dosage: 0.6 to 0.75 mg/kg, under monitoring with CBC



Herpes Zoster (Shingles)

Pain - The most frequent symptom and may precede the rash

Usually described as "burning", "throbbing", or "stabbing"

Allodynia may occur.

Erythematous maculopapular rash that quickly evolves into vesicular lesions

Vesicles are initially clear.

Pustulation and rupture typically occur after 3 or 4 days.

Crusting and involution typically occurs between day 7 and 10.

Lesions may become necrotic, generalized, or may not be present at all.

Additional symptoms:

Fever, headache, and fatigue

Paresthesia and itching

Other pain management:

Lidocaine (Xylocaine) gel x Apply to affected area every 4 to 12 hours as needed.

Calamine lotion may be used on open lesions to reduce pain and pruritus.

Capsaicin cream: Once the lesions have crusted over, capsaicin cream may be applied.

Oral corticosteroids: The addition of an orally administered corticosteroid can provide modest benefits in reducing the pain of herpes zoster and the incidence of postherpetic neuralgia.

Ocular Involvement: Herpes ophthalmicus

Ophthalmologic consultation is usually recommended

Aciclovir (Zovirax, Lovir) eye ointment x Twice daily

Rx

1. Tab. Aciclovir 400mg, 800mg (Acylex, Aclovir, Santovir, Zovirax)

» Dosage: 800mg x 5 times a day for 5-7 days. (4000mg/day)

» N.B. Increase fluid/water intake as acyclovir associated with crystal nephropathy.

ALTERNATIVE: Valacyclovir, Famciclovir but least effective

OR Tab. Valacyclovir 500mg (Valtrex, Dovirel) at dose of 1000mg (2 tablets) x Three times a day for 7 days.

OR Tab. Famciclovir 250mg (Famvir, Viracure) at dose of 500mg (2 tablets) x Three times a day for 7 days.

2. Aciclovir Ointment (Acylex, Zovirax)

Local application on affected site x Twice daily

Oral Corticosteroids used in conjunction with acyclovir has been shown to reduce the pain associated with herpes zoster.

3. Tab. Prednisolone (Deltacortril, Rapicort)

Dosage: 30 mg orally twice daily on days 1 through 7; then 15 mg twice daily on days 8 through 14; then 7.5 mg twice daily on days 15 through 21. (Ref: aafp guidelines)

Anticonvulsants often used to control Neuropathic pain

4. Tab. Carbamazepine 200mg (Tegral, Terol, Seizunil)

Dosage: 100 mg orally at bedtime; increase dosage by 100 mg every 3 days until dosage is 200 mg three times daily or response is adequate (Ref: aafp guidelines)

OR Cap. Gabapentin 100mg or 300mg (Gabix, Neogab, Gaba)

Dosage: 100 to 300 mg orally at bedtime; increase dosage by 100 to 300 mg every 3 days until dosage is 300 to 900 mg three times daily or response is adequate. (Ref: aafp guidelines)

Tricyclic antidepressants can be effective adjuncts in reducing the anxiety/depression and controlling neuropathic pain

5. Tab. Amitriptyline 25mg (Tryptanol, Amyline, Amitin)

OR Tab. Nortriptyline 25mg (Sensival)

Dosage: 25mg orally at bedtime; increase dosage by 25mg every 2 to 4 weeks until response is adequate

Maximum dose: Titrated up to 150mg per day



ATOPIC DERMATITIS/ATOPIC ECZEMA

- Atopic dermatitis is a chronic, itchy skin condition that is very common in children but may occur at any age.
- It is also known as eczema and atopic eczema and was formerly known as Besnier prurigo.
- It is the most common form of dermatitis.

△ Atopic dermatitis/atopic eczema

C/C:

Main symptoms: intense pruritus and dry skin

Infantile AD (age < 2 years)

- » Eczema: over the face, head, and extensor surfaces of the extremities that usually spares the diaper area
- » May begin as cradle cap
- » Dennie-Morgan fold: increased folds below the eye
- » Occasionally, lesions appear on the trunk.

Childhood AD (age 2 to 12 years)

- » Eczema: flexural creases (antecubital fossa and popliteal fossa), skin folds, extensor surface of hands
- » Lesions usually become Lichenified (thickening of the skin with accentuated skin markings)

Adult/adolescent AD (age > 12 years)

- » Lichenified lesions and pruritus of flexor surfaces of the extremities
- » The antecubital fossa is frequently involved.
- » Adult AD may also present as nummular eczema.

ASSOCIATED FINDINGS

- » Atopic triad: triad of asthma, allergic rhinitis, and atopic dermatitis that is linked to allergen-triggered IgE-mast cell activation
- » Food allergies
- » Xerosis
- » White dermographism: a physical finding of transiently blanched skin after skin stroking
 - Caused by cutaneous vasoconstriction
 - Normal variant, but more common in patients with atopic dermatitis
- » Dermatographism: formation of urticaria after minor pressure is applied to the skin, likely mediated by local histamine release
- » Hertoghe sign: thinning or loss of the outer third of the eyebrows
- » Keratosis pilaris: keratinized hair follicles ("rough bumps") typically distributed over extensor arms and thighs.

Rx

General measures

Avoid triggers:

- » Allergic trigger factors (pets, dust mites, pollen, certain foods)
- » Irritants (clothing, chemicals)
- » Heat
- » Keep the skin moist
- » Manage/eliminate stress
- » Breastfeeding recommended during infancy

Mild Atopic Dermatitis

- » Emollients cream or body lotion
- » Topical steroids (mild potency): Hydrocortisone 1% cream OR Fluocinolone cream (Synalar) x Apply topically on affected side twice daily.

Moderate Atopic Dermatitis

1. Emollients cream or body lotion x Use on skin after bath.
2. Topical steroids (intermediate potency) x apply twice daily.
 - » Betamethasone cream or ointment (Betnovate, Provatel)
 - OR Fluticasone cream or ointment (Cutivate, Ticovate)
 - OR Mometasone cream (Hivate, Santomet)
3. Oral antihistamines for itching/pruritis
 - » Tab. Cetirizine 10mg (Zyrtec, Rigix) x OD/BD
 - OR Tab. Levocetirizine 5mg (T-day, Belair, Xyzal) x OD/BD
 - OR Tab. Loratadine 10mg (Lorin-NSA, Softin) x OD/BD
4. If still not responding than add Topical calcineurin inhibitors
Tacrolimus 0.1% Ointment (Crolimus, Eczemus)

Severe Atopic Dermatitis

- » Emollients cream or body lotion
- » Topical steroids (high potency)
 - » Clobetasol Cream or ointment (Clobevate, Dermovate)
- » For itching/pruritis
 - » Tab. Cetirizine 10mg (Zyrtec, Rigix)
 - OR Tab. Loratadine 10mg (Lorin-NSA, Softin, Lormax)
 - OR Tab. Levocetirizine 5mg (T-day, Belair, Xyzal)
- » Topical calcineurin inhibitors
 - » Tacrolimus 0.1% Ointment (Crolimus, Eczemus)
- » Phototherapy (Narrowband UVB)
- » If not respond than hospitalize the patient and start systemic therapy: Tab. Prednisolone, Tab. Azathioprine

ALLERGIC CONTACT DERMATITIS

△ Allergic contact dermatitis

- Intensely pruritic, erythematous, papular
- Vesicles and serous oozing in severe cases
- Can spread to other parts of the body through antigen transfer by the hands or in the circulation.

Etiology

- Poison ivy, poison oak, poison sumac (urushiol-induced contact dermatitis).
- Latex or rubber gloves
- Nickel, cobalt, chromium
- Perfumes, soaps, cosmetics

Pathophysiology

- First contact with allergen → sensitization
- Repeated contact with allergen → development of a rash after 12 – 48 hour

Diagnosis is based on clinical findings

Patch test: testing for specific allergens in allergic contact dermatitis



TREATMENT OF ALLERGIC CONTACT DERMATITIS

General treatment

- Avoidance of the allergen is the best treatment and preventative measure.
- Oatmeal Bath with lukewarm water.
- Skin moisturizer
- Soothing lotions: Calamine Lotion
- Wet dressings (especially for oozing, crusting lesions)

Acute phase - Mild to moderate cases:

1. Topical corticosteroids

- » Betamethasone Cream or ointment (Betnovate, Prostate)
 - » OR Fluticasone cream or ointment (Cutivate, Tioivate)
 - » OR Clobetasol cream or ointment (Clobex, Dermovate)
- Topical application on affected area x Twice daily

Topical Tacrolimus: when corticosteroids are contraindicated

2. Oral antihistamines for itching/pruritis:

- » Tab. Loratadine 10mg (Softin, Lorin NSA, Lormax)
 - » OR Tab. Cetirizine 10mg (Rigix, Zyretic)
 - » OR Tab. Levocetirizine 5mg (T-day, Belair, Xyzal)
- Once or twice daily (OD/BD)

Severe cases: widespread, severe disease or involves mucosa

1. Tab. Prednisolone 5mg (Deltracortil, Epicort)
OR Tab. Dexamethasone 5mg (Kanadex)
2. Tab. Fexofenadine 120mg or 180mg (Fexet, Telfast, Fexo)
OR Tab. Desloratadine 5mg (Larinex, Desora, Destina)
OR Tab. Levocetirizine 5mg (T-day, Belair, Xyzal)
0 – 0 – 1 (Once daily)



DIAPER DERMATITIS (NAPPY DERMATITIS/PAMPER RASH)

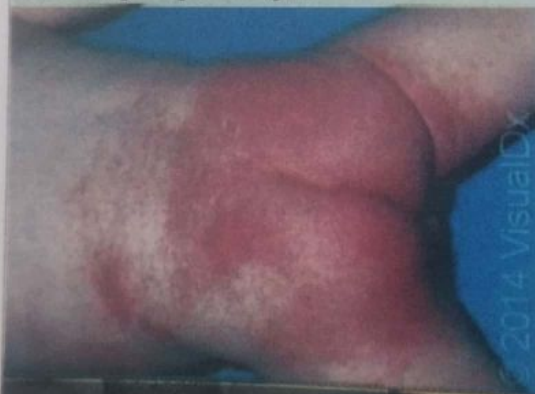
△ Diaper dermatitis C/C:

- » Diaper rash is a general term that describes any inflammatory skin eruption in the diaper covered area.
- » Rashes in the diaper area are one of the most common problems encountered in infants and toddlers, representing 10-20% of all skin disorders
- » Peak incidence occur between 9-12 months.
- » The rash can start out as a primary candidal infection or develop as a complication from irritant contact dermatitis

Presentation

- ☞ Beefy red rash with satellite papular lesions and superficial pustules that leave a collarette of scale once ruptured
- ☞ Pruritus
- ☞ Painful if there is significant maceration
- ☞ easily irritated

To distinguish from Irritant Contact Dermatitis, Candida will usually involve inguinal creases, with discrete/separate satellite pustules and papules, and scaling along the margins.



Rx

TREATMENT OF DIAPER DERMATITIS

Trigger/Causes

- ☞ Caused or worsened by the diaper
- ☞ Prolonged contact and friction of soiled diapers irritates sensitive skin.
- ☞ Using scented or harsh soaps, chemicals or detergents can also irritate the skin.

Counselling

- ☞ **Changing the diapers promptly:** Allowing an infant to remain in a wet or soiled diaper when they have a rash can make the symptoms worse.
- ☞ Switching diaper brands.
- ☞ **Avoiding using baby wipes:** may contain irritants
- ☞ Trying an oatmeal bath.

Topical antifungal therapy

1. Clotrimazole Cream (Canesten, Clotrim)
OR Ketoconazole Cream (Nizoral, Conaz)
Apply twice daily

Alternative OR If not respond to single topical therapy

Indications Topical corticosteroids

- ☞ Adjunctive therapy for symptomatic relief
- ☞ Should be used with antifungal topical therapies
- 1. Isoconazole + Diflucortolone cream (Travocort)
OR Miconazole + Hydrocortisone cream (Daktacort)
OR Clotrimazole + Hydrocortisone cream (Hydrozole)
Apply twice daily

Other over the counter available brand for nappy rash

- ☞ Dexpanthenol (Bepanthen Ointment)
- ☞ Zinc Oxide + Benzalkonium (Rashnil Cream)

POMPHOLYX (DYSHIDROTIC ECZEMA)

- Definition:** Pompholyx, also known as dyshidrotic eczema, is a vesiculobullous disease that affects the palmoplantar skin, a condition characterized by a recurrent, acute blistering eczema of the palms and/or soles. It commonly affects people aged 20 to 40.
- Etiology:** Pompholyx is associated with tinea pedis, atopic dermatitis, allergic contact dermatitis, adverse drug eruption and hyperhidrosis. It may be aggravated by hot weather, irritants, smoking or stress.
- Clinical features:**
- Acute, recurrent episodes of pruritic tapidoc-like, vesicular/bullous eruptions on the palms, lateral aspects of the fingers, and/or soles
 - Warm weather exacerbates symptoms.
 - The lesions are usually multiple and deep-seated.
 - Severe cases include dystrophic nail changes (e.g., color changes, ridge formation)
 - It typically peels off after a few weeks.
 - Secondary bacterial infection is not uncommon.
- Diagnosis:** Diagnosis is based on clinical findings.

TREATMENT OF POMPHOLYX (DYSHIDROTIC ECZEMA)

- General treatment**
 - Identify and reverse any aggravating factors.
 - Avoid triggers (e.g., allergens and irritants such as metals, perfumes, or cigarette smoking)
 - Appropriate skin care (i.e., wash hands with lukewarm water and soap-free cleanser, apply emollients after drying hands adequately)
 - Consider adding PUVA or UVA treatment for patients with refractory disease.
 - Liberal application of ointment-based emollients is also essential.
 - Corticosteroids: Potent or highly potent topical steroids are the cornerstone of treatment. In severe cases topical PLUS oral corticosteroids
- Topical corticosteroids:** Fluticasone 0.05% ointment/cream (Cutivate, Tioivate) OR Betamethasone 0.05% ointment/cream (Clobivate, Dermovate, Clobaderm) OR Clobetasol 0.05% ointment/cream (Clobivate, Dermovate, Clobaderm). Apply sparingly to the affected area(s) twice daily (BD).
- Oral antihistamines for itching/pruritis**
 - Tab. Cetirizine 10mg (Zyrtec, Rixid)
 - OR Tab. Levocetirizine 5mg (T-day, Belair, Xyzal)
 - OR Tab. Loratadine 10mg (Lorin-NSA, Softin, Lormax)
- Oral corticosteroids:** If indicated (severe disease/unresponsive to topical)
 - Tab. Betamethasone 0.5mg (Betnilon, Betnisol)
 - OR Tab. Prednisolone 5mg (Detacortil, Rapicort)



HYPERHIDROSIS

- Definition: a condition of localized or generalized excessive sweating that causes a person to sweat much more than is physically necessary in one or more parts of the body.
- Sweating is an essential bodily function that helps to regulate body temperature and prevent the body from overheating. People with hyperhidrosis have overactive sweat glands that produce more sweat than required to cool the body. Although hyperhidrosis is not a dangerous condition, it can be a source of significant stress and social embarrassment for some individuals, as it can interfere with their everyday activities and personal relationships.

Etiological classification: can be classified as primary or secondary, depending on the underlying cause.

Primary (focal) hyperhidrosis: not a symptom of underlying condition, or side-effects » Overstimulation of sympathetic nerve fibers » Causes sweat in focal areas of the body ▪ Axillary → sweaty under arms ▪ Palmar → sweaty Hands ▪ Plantar → sweaty Feet ▪ Craniofacial → Sweaty Face or Head	Secondary hyperhidrosis: » Endocrine disorder (due to hyperthyroidism, Diabetes mellitus) » Infections » Cancer » Neurological condition » Obesity, or adverse effects of medication » Substance use symptoms
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Clinical features

Excessive sweating that interferes with activities of daily living, frequent skin infections (Tinea pedis)

- » **Primary (focal) hyperhidrosis:** not a symptom of underlying condition, or side-effects
 - Overstimulation of sympathetic nerve fibers
 - Both sides of the body are affected.
 - No sweating during sleep; sweating begins immediately after waking up.
 - Usually localized (e.g., underarms, forehead)
- » **Secondary hyperhidrosis:** Generalized, may occur during sleep

△ Hyperhidrosis

What Not To Miss

- » Anxiety/stress
- » Hyperthyroidism
- » Pheochromocytoma
- » Occult malignancy
- » Substance use/medication

Diagnosis

Hyperhidrosis clinical diagnosis

- » Medical history taking
- » Physical examinations
- » Minors iodine starch test
- » **Send blood test:** TSH, FBS



TREATMENT OF HYPERHIDROSIS

- » **Antiperspirants deodorants stick** (Dove, Nivea or Rexona)
 - » Commonly applied to manage axillary hyperhidrosis, but they can also be applied to the hands or feet to reduce sweating in those areas.
 - » Most antiperspirants contain small amounts of aluminum salts, such as aluminum chloride, which interact with components of sweat and form a plug that temporarily blocks sweat release.
- » **20% Aluminum chloride** (Drysol)
 - » Apply 3 times/week at bed time and use regular deodorant in the morning
 - » Make sure site is completely dry to minimize irritation
- » **Anti-depressants:** Tab. Amitriptyline 25mg x HS or Tab. Escitalopram 10mg x OD
- » **Iontophoresis**
- » **Anticholinergics:** Tab. Oxybutynin (Urobutin, Butyn) 2.5mg x OD, titrate up to 7.5–10mg daily (can do twice daily) or Tab. Glycopyrrolate (Robinul) x Start at 1mg daily, increase to 1mg twice daily over 2 weeks, continue to titrate up to 2 mg twice daily as needed, Do not exceed 2 mg three times daily
- » Botulinum toxin injections
- » Surgery (surgical removal of sweat glands or sympathectomy)
- » Laser therapy (MiraDry)

- » **Minor's iodine-starch test** may help assess the degree of excessive sweating and effectiveness of hyperhidrosis treatments. This test is performed by applying an iodine solution to the skin, followed by a thin layer of starch powder. Once sweating begins, the mixture turns dark blue in color, outlining the area affected by hyperhidrosis.
- » **Iontophoresis** is a procedure in which an electrical current is passed through skin soaked in tap water (not distilled water), normal saline (0.9%), or a solution containing an anticholinergic medication, which allows ionised (charged) particles to cross the normal skin barrier. It reduces sweating and enhances the delivery of drugs and macromolecules into and through the skin. It is safe, effective and inexpensive.

HIRSUTISM

Definition: Hirsutism is excessive androgen-dependent body or facial hair that is present in females.

Main causes/associated condition of hirsutism include:

- » Idiopathic hirsutism - presumed to be caused by increased androgen-receptor sensitivity
- » Ovarian ($\uparrow$ testosterone)
 - Polycystic Ovarian Syndrome (PCOS)
 - Ovarian Tumors (Sertoli-Leydig cell tumors)
- » Adrenal ($\uparrow$ DHEA-sulfate)
 - Congenital Adrenal Hyperplasia (CAH)
 - Cushing's syndrome
 - adrenal tumors
- » **Drug related:** cyclosporine, phenytoin and Minoxidil
- » **Obesity and Hypothyroidism:** due to $\downarrow$ in steroid-hormone binding globulin (SHBG) $\rightarrow$ results in $\uparrow$ concentration of free testosterone
- » **Aromatase deficiency:** Inability to convert testosterone to estrogen $\rightarrow$ leads to maternal virilization when present in fetus

Hirsutism

C/C:

Idiopathic hirsutism is a diagnosis of exclusion (when all of the above causes of hirsutism have been ruled out).

Diagnostic workup

- » Obtain serum free and total testosterone levels
- If elevated testosterone – obtain**
 - » Sex hormone binding globulin level
 - » DHEAs
 - » Androstenedione
 - » Serum LH, FSH
 - » Serum prolactin
 - » 17-hydroxy-progesterone level
 - » 24-hour urinary free cortisol.
- » Serum TSH level
- » HBA1C



TREATMENT OF HIRSUTISM

- » **Counsel the patient**
- » **Stop culprit medication**
- » **Topical cream therapy**
 - » **Eflornithine 13.9% Cream** (Depilus, Vaniqa, Eflagen)
 - Apply typically twice daily (BD) on unwanted facial hairs
- » **Systemic therapy**
 - » **Oral contraceptives pills: start one of the following**
 - » Ethinyl Estradiol 0.02mg + Drospirenone 3mg (Tab. Yaz)
 - » OR Ethinyl estradiol 0.03 mg. + Levonorgestrel 0.15 mg + Ferrous Fumarate 75mg (Tab. Famila-28F, Novodol)
 - » OR Desogestrel 0.15 + Ethinyl Estradiol 0.03 (Tab. Desofam)
 - Once daily start on 3rd to 7th of menstrual cycle
- » **Other systemic drugs:**
 - » Tab. Finasteride 1 to 5mg (Genesis) x OD (pregnancy category X)
 - » Tab. Spironolactone 50mg to 100mg (Aldactone) x OD
 - » Tab. Flutamide 125mg to 250mg x twice daily (pregnancy category D)
 - » Cap. Ketoconazole 400mg x OD is useful after failure of other therapies
- » **Laser hair removal**
 - » Nd:YAG for darker skin types
 - » Diode laser for lighter skin/thin hair
 - » Most effective in fair skin with dark hair
- » **Combine eflornithine with laser therapy**
- » **PEARL:** Prior to laser hair removal, no waxing, plucking, hair removal lotions or hair bleach for 4 weeks. No retinoids or glycolics for 1 week

Condition/Labs	PCOS	Ovarian Cancer	Cushing's Disease	Adrenal Carcinoma	CAH
» Testosterone	Increased	Very Increased	N/A	N/A	N/A
» LH:FSH	Increased	N/A	N/A	Increased	Increased
» DHEA-S	N/A	N/A	Increased	Increased	Decreased
» Cortisol	N/A	N/A	Increased	Decreased	Increased
» ACTH	N/A	N/A	Increased		

ANDROGENETIC ALOPECIA

Definition: A progressive, non-scarring alopecia that affects the regions of the scalp with the most androgen-sensitive hair follicles, resulting in a characteristic pattern of balding (bitemporal scalp in male and vertex & frontal scalp in female)

Epidemiology

- » Most commonest type of alopecia
- » Prevalence: increases with age (advance age), Sex: male > female
- » Age at onset: Male sex → Puberty, Female → Menopause
- » Race: more common in White individuals

Etiology

- » Increased androgen sensitivity of hair follicles in genetically predisposed individuals, Positive family history
- » Conditions that cause hyperandrogenism such as Polycystic ovary syndrome (PCOS), Insulin resistance disorders
- » Congenital adrenal hyperplasia, Androgen-producing tumors (Leydig cell tumor), Prostate cancer

Clinical features

- » General features: Gradual, non-scarring hair loss
- » Male pattern baldness
 - » Bitemporal "M" pattern of recession
 - » May be followed by hair loss on the vertex of the scalp
- » Female pattern baldness
 - » Begins at the vertex
 - » Progresses to diffuse hair thinning of the entire scalp
 - » Seen primarily in postmenopausal women
 - » Maybe accompanied by features of hyperandrogenism

Diagnostic workup

- » Trichoscopy: Follicular miniaturization
- » Negative hair pull test: Approximately 50 to 100 hairs are grasped between the thumb & the middle and index fingers & then firmly pulled. >3 hairs pulled is a +ve test
- » Women with hyperandrogenism: Refer to endocrinology
- » Laboratory test: Need to be off birth control for 1 cycle and test in the morning while menstruating.
 - » Serum total and free testosterone level
 - » Serum Dehydroepiandrosterone sulfate (DHEA-S)
 - » Serum 17-hydroxy-progesterone and Prolactin level
 - » Iron studies (serum ferritin) and serum TSH

What Not To Miss

- » Pathologic hyperandrogenism
- » Look for: Irregular menses, infertility, hirsutism, severe cystic acne, virilization, galactorrhea
- » Telogen effluvium "unmasking" underlying androgenetic alopecia

Differential diagnosis

- | | |
|---------------------------|---------------------|
| » Diffuse alopecia areata | » Syphilis |
| » Anagen effluvium | » Telogen effluvium |

5. Platelet-rich plasma (PRP) is an autologous preparation of plasma with a supraphysiologic concentration of platelets thought to promote wound healing & hair growth through the release of various growth factors from activated platelets.
6. Microneedling: With microneedling, fine needles are applied to the scalp via a roller or pen and microwounds are induced which activate wound healing and the generation of various growth factors.



Female pattern baldness



Treatment of MEN androgenetic alopecia

1. Minoxidil 5% solution (Minoxin 5% plus, Regrow 5%) x Apply 1 mL to the affected area(s) twice daily.
 2. Adjuvant: Tab. Finasteride 1mg (Genesis, Hairfin) at dose 1mg orally once daily
- ❖ Treatment duration: atleast 6 months up to 12 months

Treatment of WOMEN androgenetic alopecia

1. Minoxidil 2% solution (Minoxin 2%, Regrow 2%) x Apply 1 mL to the affected area(s) twice daily (BD).
2. Adjuvant: Tab. Finasteride 1mg (Genesis, Hairfin) x at dose 1 mg orally once daily, Off-label use in women
3. Female patient with hyperandrogenism
 - » Tab. Spironolactone 100mg (Aldactone) at dose 200mg orally once daily for at least 12 months.
 - OR Tab. Flutamide 250mg x once daily (OD).
 - » AND Drospirenone/ethinyl estradiol (Tab. Yaz) OR Cyproterone acetate/ethinylestradiol (Dian 35) x OD

NON-PHARMACOLOGICAL MEASURES

1. Patient support and psychological counselling
2. Cosmetic hair camouflage: Cosmetic aids such as tinted cosmetics, hair lightening, and creative hair styling may help to camouflage the defect. Hairpieces, wigs or hair extensions may also cover the scalp.
3. Low-level laser treatment: self-administered via combs or caps – devices to help grow hair.
4. Hair transplant surgery: Follicular units from the occipital scalp are extracted (either as small units or as a linear strip), divided into small units, & implanted into the bald areas



male-pattern baldness



ALOPECIA AREATA

Definition: Alopecia areata (AA) is an autoimmune disease that causes inflammation of the hair follicles resulting in non-scarring hair loss, affecting scalp and body hair.

Prevalence: = 1 in 1000 people, **Age of onset:** mostly < 40 years, **Sex:** male = female

Etiology:

- Unknown, immune-mediated inflammation and disruption of anagen phase hair follicles.
- A trigger factor (e.g., emotional stress, infections, pregnancy) may precede some cases.
- Family history in = 20% of cases.

CLINICAL FEATURES

- Abrupt onset (within weeks)
- Smooth, circular, well-defined patches of hair loss without scarring
- Nail involvement (up to 40% of cases):** Nail pitting, onycholysis, Beau lines.
- Other autoimmune disorders may be present (e.g., vitiligo, autoimmune thyroid disorders).

PATTERNS OF HAIR LOSS

- Ophiasis:** Hair loss localized to the back and sides of the scalp.
- Sisipho:** Sparing of the sides & back of the scalp.
- Extensive alopecia areata:** Hair loss affecting > 50% of the scalp.
- Alopecia universalis:** All hair-bearing sites are affected (mimics telogen effluvium).
- Alopecia totalis:** Complete baldness

DIAGNOSTIC WORKUP

- Laboratory test**
 - CBC with differential
 - Iron studies
 - Serum TSH
 - Serum Vitamin-D
- Trichoscopy:** exclamation point hairs
- Scalp biopsy & trichogram** may be performed to confirm the diagnosis.
- Positive Hair pull test**
- What Not To Miss:** Autoimmune thyroid disease (Hashimoto's thyroiditis), Vitiligo & IBD

TREATMENT OF EXTENSIVE HAIR LOSS

- Topical immunotherapy** may be tried with either DNCB (1-chloro-2, 4-dinitrobenzene), DPCP (Diphenylcyclopropenone), OR SADBE (squaric acid dibutyl ester).
- JAK INHIBITOR:** Baricitinib, is the 1st systemic drug to be approved by the US FDA and the European Medicine Agency to treat adults with severe alopecia areata, which reveal that oral baricitinib increased hair regrowth at 36 weeks, compared with placebo, in people with severe alopecia areata

DIFFERENTIAL DIAGNOSIS

- Trichotillomania:** Compulsive pulling out of hair resulting in ill-defined patchy hair loss and different lengths of hair
- Loose anagen syndrome:** Hair falling out in clumps with minimal traction due to abnormal keratinization of the hair root and poor anchoring of the hair follicle to the scalp.
- Tinea capitis:** Affected areas of the scalp appear scaly.
- Secondary syphilis:** The scalp has a moth-eaten appearance due to patchy hair loss.
- Brocq pseudopelade:** Irregular areas of hair loss that become scarred in later stages



TREATMENT OF LIMITED HAIR LOSS

FIRST LINE TREATMENT → OPTION INCLUDE:

- Topical corticosteroids – a three-month trial**
 - Clobetasol 0.05% ointment (Clobivate, Dermovate)
 - OR Mometasone 0.1% ointment (Hivate, Santomet)
 - Apply sparingly to the affected area(s) twice daily (BD)
 - PLUS, Cosmetic hair camouflage and Patient support (patient psychological support and counselling)
- Topical Minoxidil ± Topical corticosteroids**
 - Minoxidil 5% solution (Minoxin Plus, Hairmax Plus)
 - Apply 1 mL to the affected area(s) twice daily.
 - ± Clobetasol 0.05% ointment (Clobivate, Dermovate)
 - Apply sparingly to the affected area(s) twice daily (BD).
 - PLUS, Cosmetic hair camouflage and Patient support
- Intralesional Corticosteroids**
 - Inj. Triamcinolone acetonide 40mg/ml (K-Cort, Kenacort-A)
 - Dosage:** at dose 2.5mg to 5 mg intralesionally to brows, beard, or scalp every 4-6 weeks until full regrowth, stop if no response after 6 treatment.
 - Adjuvant: Topical Minoxidil ± Topical corticosteroids
 - PLUS, Cosmetic hair camouflage and Patient support

SECOND LINE TREATMENT

- Oral corticosteroids:** Tab. Prednisolone 5mg (Deltacortril, Rapicort) at dose at dose 30-40mg/day orally for two weeks, then taper dose gradually over the next 4 weeks for a total of six weeks treatment.
- Adjuvant: Topical Minoxidil ± Topical corticosteroids
- PLUS Cosmetic hair camouflage, Patient support and counselling



TELOGEN EFFLUVIUM (EXCESSIVE HAIR SHEDDING)

Definition: Telogen effluvium is a scalp disorder characterized by diffuse, non-scarring, temporary hair loss due to the excessive shedding of resting or telogen hair after some shock to the system. New hair continues to grow. Telogen hair is also known as a club hair due to the shape of the root.

Etiology

- » **Endocrine:** Hypothyroidism, hyperthyroidism
- » **Medication induced:** retinoids, antithyroid drugs, anticonvulsants, anticoagulants, NSAIDs, antidepressants, discontinuation of oral contraceptives.
- » **Nutritional:** zinc deficiency, iron deficiency, riboflavin deficiency, Vitamin-D deficiency, malnutrition states
- » **Stress:** severe febrile illness, emotional stress, hemorrhage (e.g., trauma, major surgery)
- » **Infectious:** Typhoid, malaria, HIV, tuberculosis, syphilis
- » **Other causes:** telogen gravidarum, autoimmune disease (e.g., systemic lupus erythematosus)

Mechanism: Telogen (resting) phase of hair growth predominates → premature shedding of the resting hair follicles → diffuse, nonscarring hair loss.

Clinical features

- » Hair density reduces by < 50%.
- » Does not progress to complete baldness.

Diagnostic workup

- » **Hair pull test:** positive
- » **Trichogram:** > 25% of hairs in the telogen phase
- » Assessment for potential triggers 2–5 months prior to the onset of hair loss
- » Scalp biopsy if uncertain (rarely necessary)



TREATMENT OF TELOGEN EFFLUVIUM (EXCESSIVE HAIR SHEDDING)

Reassurance the patient

Addressing Underlying Causes

- » **Identify and Manage Triggers:** Determine and address any triggering factors such as stress, illness, medication, hormonal changes, or nutritional deficiencies.
- » **Medication Review:** Evaluate current medications and consider alternatives if a drug is identified as a trigger.
- » **Hormonal Imbalance:** Treat any underlying hormonal imbalances that may contribute to telogen effluvium, often through hormone replacement therapy or other targeted treatments.
- » **Nutritional Deficiencies:** Correct deficiencies in iron, vitamin D, B vitamins (especially biotin), and other essential nutrients crucial for hair health.

Promoting Hair Growth and Health

- » **Nutritional Supplements:** Consider supplements like biotin, zinc, iron, and vitamin D, as recommended by a healthcare provider based on lab tests and nutritional status.
- » **Topical Treatments:** Use topical minoxidil (Rogaine), which is FDA-approved to promote hair growth, though effectiveness in telogen effluvium may vary.
- » **Avoiding Hair Damage:** Gentle hair care practices, such as avoiding excessive heat styling, harsh chemicals, and tight hairstyles that can further damage fragile hair.
- » **Scalp Care:** Maintain a healthy scalp with regular washing using a mild shampoo and gentle massaging to promote circulation.

Psychological Support: Coping Strategies – Provide support and resources for coping with the emotional impact of hair loss, which can be distressing for many individuals.

Regular follow-up and Monitoring: Monitor progress and adjust treatment as needed based on response and any changes in underlying health conditions.

Professional Advice: Always consult with a healthcare provider or dermatologist for personalized evaluation and treatment recommendations tailored to your specific condition and medical history. They can provide guidance on the most effective strategies for managing telogen effluvium based on the underlying causes and individual needs.

BURN

ETIOLOGY

Thermal burns (most common):

1. Flame burns: Fire.
2. Contact burns: Hot surfaces.
3. Scalding: Hot liquids or steam.

Non-thermal burns:

1. Chemical burns

- » **Acids:** sulfuric acid (e.g., in lead acid batteries), nitric acid (e.g., explosives and polymer industry), hydrofluoric acid (e.g., in cleaning products for electronics), phenol, and acetic acid
- » **Alkalis:** anhydrous ammonia (e.g., in fertilizers), calcium oxide (e.g., in cement), sodium hydroxide, and potassium hydroxide
- » **Miscellaneous:** white phosphorus (e.g., in fireworks), metals (e.g., sodium, potassium, lithium), bleaching agents (e.g., hydrogen peroxide, hypochlorite), vesicants (e.g., mustard gas), hydrocarbons (e.g., gasoline, diesel fuel)

2. Electrical burns

- » **Low-voltage sources:** electrical cords, outlets in households
- » **High-voltage sources:** power lines, lightning

3. Radiation burns

- » **Electromagnetic waves**
 - **UV radiation:** from sunlight, phototherapy
 - **X-rays, gamma rays:** from radiotherapy, radio-diagnostic procedures, nuclear accidents
 - **Infrared waves:** from warming lamps and microwaves
- » **High-energy particles (e.g., from radiotherapy, nuclear accidents):** alpha particles, beta particles, high-energy neutrons

4. Friction burns: skin injury caused by abrasion against a hard surface (esp. at high speeds) and the heat generated by the resulting friction (e.g., from skidding across the street due to a motorcycle accident)

CLASSIFICATION DEPTH OF BURNS

1st degree burns (superficial burn)

- » **Affected tissue layers:** Superficial layers of the epidermis.
- » **Pain:** YES – painful (Localized pain).
- » **Wound blenching on pressure:** YES → Rapid refill.
- » **Appearance:** Similar to sunburn. **Localized features:** erythema, swelling, skin appears dry, no blistering.
- » **Prognosis:** Healing within 3–6 days. No scarring.

2nd degree burns (partial thickness burn)

2-a (superficial partial thickness burn)

- » **Affected tissue layers:** Epidermis and upper layers of the dermis (papillary dermis)
- » **Pain:** YES – Pain especially with the movement of air or changes in temperature in the area surrounding the wound.
- » **Wound blenching on pressure:** YES → Slow refill
- » **Appearance:** Erythema, Swelling, Increased temperature of affected skin, Vesicles/bullae
- » **Prognosis:** Healing within 1–3 weeks, Temporary hypopigmentation/hyperpigmentation, No scarring

2-b (deep partial thickness burn)

- » **Affected tissue layers:** Deeper layers of the dermis (papillary and reticular dermis)
- » **Pain:** YES – Pain is typically felt on applying pressure
- » **Wound blenching on pressure:** NO → Very slow refill
- » **Appearance:** Vesicles/bullae: fragile (rupture easily), Mottled coloration of the skin with red and/or white patches
- » **Prognosis:** Healing takes 3 weeks or longer. Moderate to high risk of hypertrophic scarring.

3rd degree burn (full thickness burn):

- » **Affected tissue layers:** Epidermis, dermis, and subcutaneous tissue.
- » **Pain:** NO – Perception of deep pressure is intact.
- » **Wound blenching:**

- ☞ **Appearance:** Tissue necrosis with black/cherry red, waxy-white, or gray leather-like skin (eschar), skin appears dry and inelastic.
- ☞ **Prognosis:** The burn does not heal by itself. Need grafting.
- ☞ **4th degree burns (deeper injury burn):**
- ☞ **Affected tissue layers:** Epidermis, dermis, and deeper structures (muscles, fat, fascia, and bones)
- ☞ **Pain:** NO – Minimal perception of deep pressure)
- ☞ **Wound blanching on pressure:** NO → Very slow refill
- ☞ **Appearance:** Similar to third-degree burns
- ☞ **Prognosis:** The tissue is dead and requires amputation/need grafting.

Burn extent - Assessment of burn surface area involvement

Total body surface area (TBSA) is the total area of skin involved in an injury (e.g., burn) or disease (e.g., psoriasis). TBSA is calculated using tools such as the Lund-Browder chart & the rule of nines to assess the severity of the skin condition.

1. **Rule of nines:** A simpler clinical tool used to rapidly assess the extent of body surface area affected by burns in adults. Divides the adult body's surface into 11 regions (head/neck, 2x anterior trunk, 2x posterior trunk, each arm, 2x each leg), each of which comprises ~ 9% of the total body surface. or plus 1% for the genital/perineal region. The rule of nines does not accurately account for pediatric proportions in children.
2. **Lund-Browder chart:** Most accurate method for both adults and children. A set of charts that take into account the different proportions of children and adults (children have proportionally up to 20% larger heads and up to 13% smaller legs) to more precisely estimate the burn surface area involved.

BODY SURFACE AREA ESTIMATION

Segment	Adult	Small child	Infant
» Head	9%	16%	18%
» Trunk	36% (4 x 9%)		
» Arms	18% (2 x 9%)		
» Thighs	18% (2 x 9%)	14.5%	13.5%
» Lower legs and feet	18% (2 x 9%)	14.5%	13.5%
» Genital region	1%		

CLASSIFICATION OF BURN SEVERITY

1. Minor burn	» Partial thickness burns < 10% TBSA in adults » Partial thickness burns < 5% TBSA in children or older adults » Full thickness burns < 2% TBSA in any patient without other injuries
Management: Outpatient (OPD) treatment	
2. Moderate burn	» Partial thickness burns 10–20% TBSA in adults » Partial thickness burns 5–10% TBSA in children or older adults » Full thickness burns 2–5% TBSA » Any of the following: ☞ Low-voltage electrical burn ☞ Suspected inhalation injury ☞ Circumferential burn ☞ Comorbidities that increase infection risk (e.g., diabetes mellitus)
Management: Hospitalization admission	
3. Major burn	» Partial thickness burns > 20% TBSA in adults » Partial thickness burns > 10% TBSA in children and older adults » Full thickness burns > 5% TBSA » Any of the following: » High-voltage electrical injury ☞ Chemical burns ☞ Inhalation injury ☞ Burn to the face, eyes, ears, hand, feet, genitalia, or perineum ☞ Burns around major joints ☞ Other concomitant significant trauma (e.g., fractures)
Management: Refer to burn center	

DIAGNOSTIC APPROACH TO THE BURN PATIENT

- ☞ **History & Exam:** Burn severity is based on clinical history and physical examination, but further testing may be necessary to monitor for complications and guide therapy.
- ☞ **Pulse oximetry:** To monitor for hypoxemia. In circumferential limb wounds, assess perfusion via pulse oximetry (> 90% indicates adequate perfusion), capillary refill, and peripheral pulses to monitor for ischemia and compartment syndrome.
- ☞ **Blood tests**
 - » **Arterial blood gas (ABGs):** to monitor for hypoxemia, may show metabolic acidosis in inhalation injury

- » CBC: Low Hb, RBCs & Hct (to monitor for hemolysis), Neutropenia & thrombocytopenia (indicate sepsis).
- » Serum electrolytes: to monitor for hyperkalemia and hyponatremia in the acute phase and hypernatremia in the post-acute phase.
- » Blood glucose level: stress induced hyperglycemia
- » BUN/creatinine: to monitor for acute renal injury → High level.
- » Serum protein and albumin levels: to monitor for hypoalbuminemia in the acute phase.
- » Wound swab and blood cultures: in suspected wound infection or sepsis.

TREATMENT OF MINOR BURNS

- Rx**
- » Management of the burn area
 - » Remove clothing, dirt, and debris.
 - » Cool with room-temperature or cool running water.
 - » Wound care
 1. Irrigation: cleaning the wound with mild soap and water
 2. Topical moisturizers (e.g., calamine lotion, aloe vera-based gels): symptom relief for 1st-degree burns
 3. Consider derroofing blisters.
 4. Consider antiseptic ointments (e.g., silver sulfadiazine) or topical antibiotics (e.g., bacitracin, Fusidic acid) for 2nd-degree burns PLUS Lidocaine 2% jelly (Xylocaine jelly)
 5. Wound dressing is indicated in 2nd-degree burns
 - » Types of dressings: paraffin-impregnated gauze (Paragaz, Surge wax), hydrocolloid dressing, biosynthetic dressing
 - » Wet-to-dry dressing: for infected wounds or wounds with devitalized tissue
 - » Pain management: Tab. Paracetamol 500mg (Panadol, Calpol) at dose 500-1000mg 3-4 time a daily OR Tab. Diclofenac sodium 50mg (Voren, Voltral) 2-3 time daily
 - » Tetnus prophylaxis: tetanus vaccination – Inj. Imatet 0.5 ml x IM

TREATMENT OF MODERATE & MAJOR BURNS

- Rx**
- » Stabilize patients using ABCD&E approach.
 - » Airway: Ensure airway patency. Be prepared for intubation if there is airway compromise or inhalation injury. Intubation is indicated if an inhalation injury is suspected or if burns involve > 30% TBSA. Do not delay intubation if needed, as fluid resuscitation can increase laryngeal swelling.
 - » Breathing: Assess breathing and provide supplemental oxygen. Consider escharotomy if circumferential chest burns restrict breathing.
 - » Circulation: Establish IV access, preferably two large-bore IVs. Begin fluid resuscitation.
 - » Disability: Assess neurological status.
 - » Exposure: Remove all clothing and jewelry. Assess the extent of burns and associated injuries.
 - » Vitals monitoring: Check Blood pressure, Pulse, Respiration, Temperature, SpO₂.
 - » Obtained labs: CBC, BUN, Creatinine, Electrolytes, LFTs, RBS, PT, INR, ABGs
 - » IV fluid resuscitation with crystalloid solution: Ringer lactate (R/L) – Fluid of choice
 - » Revised fluid resuscitation protocol for severe burns: The volume for 24 hours of initial fluid therapy with Ringer's Lactate solution (RL) is calculated using the **Parkland formula**:

$$4 \text{ mL} \times [\% \text{ of total body surface area (TBSA) affected by 2nd-degree and 3rd-degree burns}] \times \text{weight (in kg)}$$
 - » Adjustments to the parkland formula: To minimize the risk of serious complications from over resuscitation (e.g., pleural effusion and compartment syndrome), the Advanced Trauma Life Support (ATLS) and American Burn Association guidelines recommend the following adjustments:
 - » Individuals ≥ 14 years of age: Use half the volume calculated using the Parkland formula.
 - » Individuals < 14 years of age who are ≥ 30 kg: Initial fluid therapy with ringer lactate (RL) for a 24-hour period using $3 \text{ mL} \times [\% \text{ of TBSA affected by 2nd-degree and 3rd-degree burns}] \times \text{weight (in kg)}$.
 - » Children < 30 kg: Provide 24 hours of initial fluid therapy followed by 24 hours of maintenance fluid therapy with a glucose-containing solution.
 - » Administration Schedule
 - » Administer half of the recommended fluid volume within the first 8 hours.



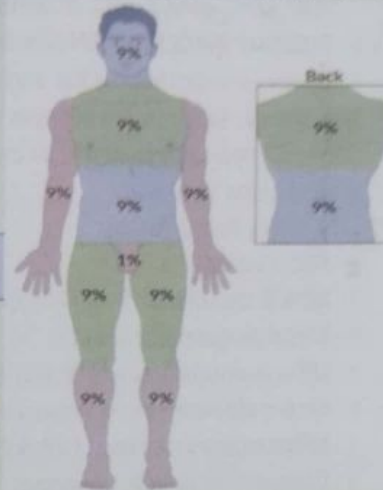
- Administer the remaining half over the course of the next 16 hours.
 - » **Additional consideration:** Combining crystalloids with colloids (e.g., albumin, plasma) or high-dose vitamin-C can help reduce fluid requirements. Following initial stabilization, patients who need aggressive fluid resuscitation should have a urethral catheter placed to monitor urine output and adjust fluid therapy as necessary.
- ☛ **Treatment of burn area:**
 - » **Initial Steps:** Remove clothing, dirt, and debris from the burn area. Clean the burn wound with saline.
 - » **Dressing:** Apply appropriate dressings to maintain a moist wound environment and protect against infection. **Options include** silver sulfadiazine, hydrocolloid dressings, and biologic dressings.
 - » **Cooling the Burn:** Cool the burnt area with room-temp. or cool running water or saline-soaked gauze.
 - » **Escharotomy/Fasciotomy:** if there is evidence of compromised circulation due to circumferential burns.
 - » **Temperature Monitoring:**
 - ☛ Monitor the core body temperature for hypothermia.
 - ☛ If the body temperature is $< 35^{\circ}\text{C}$, administer warm IV fluids.
 - » **Caution with Large Burns:** For patients with burns $> 10\%$ TBSA, cool with caution or avoid cooling altogether due to the high risk of hypothermia.
- ☛ **Continuing management of severe burns**
 - » **Indications for treatment in a specialized burn unit**
 1. 2nd-degree burns involving $> 10\%$ TBSA
 2. 3rd-degree burns involving $> 5\%$ TBSA
 3. Burns due to inhalation injury
 4. Burns involving hands, feet, genitalia, or major joints
 5. Burns with High-voltage electrical or chemical burns
 - » **Wound care**
 1. **Early debridement:** Prompt removal of necrotic tissue.
 2. **Wound Dressing Options:**
 - ☛ Free-skin grafts (split thickness or full thickness)
 - ☛ Flap reconstruction (free or pedicled flaps)
 - ☛ Topical antibiotics (e.g., silver sulfadiazine, bacitracin, neomycin)
 - » **Nutritional Support**
 - ☛ **Preferred Method:** Enteral feeding via nasogastric or nasoduodenal tube.
 - ☛ **Early Initiation:** Crucial to manage hypermetabolic response.
 - » **Pain and Anxiety Management**
 - ☛ **Pain Relief:** NSAIDs and opioids as needed.
 - ☛ **Anxiety Control:** Benzodiazepines (Diazepam) for acute distress.
 - » **Prophylactic Measures**
 - ☛ **Stress ulcer prophylaxis:** Proton pump inhibitors or H_2 antagonists.
 - ☛ **Tetanus prophylaxis:** tetanus vaccination – Inj. Imatet 0.5 ml x IM
 - » **Antibiotic Management:** Avoid routine prophylactic antibiotics. Start empiric therapy (e.g., vancomycin, cefepime for *Pseudomonas*) if infection is suspected.
 - » **Physical Therapy:** Essential for maintaining mobility and function.
- ☛ **Specific Considerations**
 - » **Eschar management**
 1. **Circumferential eschar:** Perform a Doppler test and check capillary refill time, peripheral pulses, sensation, and pulse oximetry in the limb hourly for 24–48 hours to assess for vascular/respiratory compromise or compartment syndrome.
 - ☛ **No vascular/respiratory compromise or compartment syndrome**
 - Raise the legs or upper body
 - Perform a range-of-motion exercises as tolerated
 - ☛ **Vascular/respiratory compromise or compartment syndrome**
 - **Escharotomy:** an incision of the burnt necrotic tissue to prevent constriction of the skin
 - **Fasciotomy** is indicated if compartment syndrome develops.
 2. **Chest/neck eschars:** escharotomy in impending or active respiratory compromise
 - » **Chemical burns:** Immediate, copious irrigation of all areas of exposure.

STEVENS-JOHNSON SYNDROME (SJS)

- Stevens-Johnson syndrome (SJS): It is rare, immune-mediated skin reaction that leads to extensive epidermal detachment with mucocutaneous complications and is associated with a high mortality.
- Stevens-Johnson syndrome (SJS) is a less severe manifestation of toxic epidermal necrolysis (TEN)
- SJS & TEN are the same entity but differ in terms of disease severity (based on surface area of skin involved)
- Sex ratio: More common in female than male (5:3).

Cutaneous Involvement Spectrum - clinically accepted classification

- It dependent on total body surface area (TBSA) involvement:
 - SJS: <10% TBSA involvement
 - SJS/TEN overlap: 10% to 30% TBSA involvement
 - TEN (severe SJS): >30% TBSA involvement



TRIGGERS/ETIOLOGICAL FACTORS

- Idiopathic
- Drugs (most common trigger, = 80% of cases)
 - Corticosteroids
 - Antiretroviral drugs (nevirapine, abacavir) & antivirals (acyclovir)
 - Antibiotics: sulfonamides (TMP/SMX), penicillins, cephalosporins
 - Fluoroquinolones (ciprofloxacin, Levofloxacin), and Anti-tuberculosis (isoniazid, rifampin, pyrazinamide)
 - Antiepileptics: phenytoin, phenobarbital, lamotrigine, valproic acid, carbamazepine, ethosuximide
 - Other: Allopurinol, sulfasalazine, azathioprine, anti-malarials, oxicam NSAIDs (piroxicam), retinoids, anticancer drugs, tranexamic acid, metronidazole, furosemide, diazepam and anthelmintics
- Infections: SJS can be a sequela of several conditions, including: URTI, Pharyngitis, Otitis media, mycoplasma pneumoniae, herpes, Epstein - Barr virus (EBV) and cytomegaloviruses (CMV).
- Rarely: vaccinations (smallpox), graft-versus-host disease
- Risk factors: Patients with active cancer anticonvulsant medications, recent infection recent antibiotic use, systemic lupus erythematosus (SLE), HIV-positive, radiation therapy, HLA and genetic predisposition.

PATHOPHYSIOLOGY

Pathogenesis is not completely understood but is thought to involve a **delayed type-IV HSR**: ↑ activity of drug-specific cytotoxic T cells → release of granulysin; (a cytolytic protein) by an unknown mechanism → damage to keratinocytes

CLINICAL FEATURES

- Prodromal phase (begins 1–3 weeks after the intake of medication): high fever usually 102°F (> 39°C), malaise, sore throat, myalgia and/or arthralgia
- Mucocutaneous lesions appear 1–3 days after the onset of prodromal symptoms
 - Cutaneous manifestation sequence
 - Painful, erythematous/purpuric macules
 - May have a targetoid appearance (cockade lesions)
 - Typically seen over the face and trunk
 - Lesions form bullae and/or vesicles; **POSITIVE** Nikolsky sign
 - Extensive, full-thickness epidermal necrosis and sloughing (resembling large superficial burns)
 - Healing by re-epithelialization: begins 1–2 weeks after epidermal sloughing and is completed within a few weeks
 - Mucosal membranes: almost always involved
 - Oral and pharyngeal mucosa: stomatitis, cheilitis, oral ulcers, odynophagia
 - Severe conjunctivitis, corneal ulcers: photophobia, eye pain
 - Urethritis, genital ulcers, and/or perianal ulcers
 - Esophageal ulcers and/or strictures (less common): dysphagia
 - Tracheal involvement (less common)
 - Small bowel, colon involvement (rare): diarrhea, melena, intussusception, bowel perforation

DIAGNOSTIC WORKUP

Clinical diagnosis based on characteristic clinical presentation, history (medications) and skin biopsy results are sufficient to diagnose SJS/TEN

» **History and physical examination**

- » **Rashes:** a sudden rash or a rash that develops after a new drug is started
- » **Mucosal involvement:** Erosions or ulceration of the eyes, lips, mouth, pharynx, esophagus, GIT, kidneys, liver, anus, genital area, or urethra.
- » **POSITIVE NIKOLSKY SIGN** (Epidermal layer easily sloughs off when pressure is applied to the affected area)
- » Blisters or macules and flat atypical target lesions, diffuse erythema.

» **Skin biopsy:** Keratinocyte necrosis with detachment of the epidermal layer of the skin from the dermal layer (apparent sub-epidermal split). Eosinophilic infiltration with minimal infiltration of lymphocytes & histiocytes around blood vessels

» **Laboratory investigation:**

- » CBC: Leukopenia
- » BUN & creatinine: ↑ renal injury/failure
- » Blood glucose: Increased
- » LFTs: abnormal, may be ↑ AST & ALT
- » Serum electrolytes: ↓ Potassium & sodium levels suggest volume depletion.
- » Inflammatory markers: CRP & ESR ↑
- » Coagulation profile: abnormal
- » ABGs: Hypoxemia, acidosis
- » Chest-x-ray (CXR): Possible pneumonia or interstitial pneumonitis

Rx

» Stabilize patient using ABCD&E approach.

» Establish large-bore intravenous (IV) access.

» Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂ (Check SpO₂ & Give high flow O₂ as appropriate)

» Obtained labs: CBC, BUN, electrolytes, creatinine, LFTs, blood glucose, coagulation profile, CRP, ESR & ABGs

» Identify and discontinue any offending medication: usually it will be a new medication started in the 2-3 weeks prior to onset of the rash.

» Seek an urgent dermatological and ophthalmological consult.

» Consider transfer to a burn unit in more severe cases.

» **VTE prophylaxis:** Inj. Enoxaparin sodium 80mg/0.8ml (Clexane) x at dose 100 IU/kg (or 1.5mg/kg) x SC x OD

» **Wound care:** Wound care can follow either a conservative or surgical approach to debridement depending on the needs of the individual patient.

» **Conservative management (antishear strategy) recommends:**

- ↳ Preserving the detached epidermis as a biologic dressing
- ↳ Limiting dressing changes
- ↳ Using an air-fluidized bed and non-adherent dressings
- ↳ Using lysis and drainage of wounds only for patient comfort
- ↳ Cleansing wounds with sterile water or dilute chlorhexidine when dressings are changed.
- ↳ Applying an emollient to the whole epidermis to enhance skin barrier function, reduce fluid loss, and encourage re-epithelialization.
- ↳ Considering use of a non-adherent silver-impregnated primary dressing for antibacterial properties, reduced requirement for dressing changes, and improved patient comfort
- ↳ Using secondary absorptive dressings to control exudate.

» **Surgical management:** The surgical approach for wound care for SJS/TEN patients generally follows practice in burn management;

- Once the surgical debridement of detached epidermis is achieved, wounds are covered with a biologic dressing, such as: Xenograft (pigskin), Allograft (cadaver skin), OR synthetic dressing. With healing, consider a non-adherent silver-impregnated dressing for dressing changes & improved patient comfort.
- UK guidance recommends that patients should be transferred to a burn unit for surgical debridement & wound care if they have TEN (>30% body surface area epidermal loss) & evidence of the following:
 - Clinical deterioration
 - Extension of epidermal detachment
 - Subepidermal pus
 - Local sepsis
 - Wound conversion, and/or delayed healing
- Once the skin has regenerated (after about 2-3 weeks), emollients can be useful to keep it supple and prevent drying out.

Management of pain: Analgesia should be given based on the severity of symptoms to ensure comfort at rest. Pain level should be evaluated once every 4 hours and assessed at least once daily using a validated pain tool. Patients will require more pain medication during dressing changes. NSAIDs should be avoided due to the increased risk of renal or gastric injury.

- Mild pain:** Inj. Paracetamol 1g/100ml (Provas) x IV x TDS/QID, when required (maximum 4000mg per day) OR Tab. Paracetamol 500mg (Panadol) at dose 500mg to 1000mg x orally every 4-6 hours. (max 4g/day)
If pain is not control with paracetamol, consider Opioid analgesic: Inj. Tramadol 100mg/2ml (Tramal) at dose 50-100mg x IV every 4-6 hours when required, maximum 400mg/day OR Cap. Tramadol 50mg (Tramal) at dose 50-100mg orally every 4-6 hours when required, Maximum 400mg/day.
- Moderate to severe pain:** consider morphine sulfate OR Fentanyl
 - Inj. Morphine sulfate at dose 2.5 to 10 mg IV/IM/SC, every 2-6 hours when required, OR 0.8 to 10mg/hour IV infusion, OR Cap. Morphine sulphate at dose 10-30mg orally every 4 hours when required, adjust dose according to response.
OR Fentanyl
 - PLUS, Low-dose ketamine can be considered as an alternative or adjuvant therapy for SJS/TEN pain.
- Gabapentin and Pregabalin both address neuropathic pain and may decrease opioid consumption.

FLUID RESUSCITATION & REPLACEMENT OF ONGOING FLUID LOSS

- Oral fluid:** If the patient can take fluids orally, encourage them to do so.
- IV fluid resuscitation (same as burn):** Start IV fluid therapy with crystalloids fluids, usually Ringer lactate (RL) OR 0.9% Normal saline (NS). Volume of Ringer lactate to be administered within a period of 24 h = 2 mL x % of total body surface area involved. Half of this volume should be administered within the first 8 hours and the remaining half within the next 16 hours (see management of burn explained above).
- Fluid resuscitation is monitored by urine output of 0.5 mL/kg/hour (30-50 mL/hour)
- Increase or decrease fluid resuscitation based on the urine output.
- Gastroprotective (to prevent stress-related gastritis/curling ulcer):** Inj. Omeprazole 40mg/vial (Ruling, Risek) x IV OR Cap. Omeprazole 40mg (Ruling, Risek) initially at dose 40mg, followed by 40mg in 8 hours on DAY-1, then 40mg, Per orally (PO) x Once daily (OD)
- Supportive treatment of ORAL involvement**
 - Applying petrolatum ointment on the lips every 2 hours
 - Topical oral pain management: Benzydamine (Enziclor gel) OR Viscous lidocaine (Xylocaine jelly) x before eating or oral cleansing.
 - Oral hygiene: Patient mouth should be cleaned daily with warm saline mouthwashes or an oral sponge.
 - Antiseptic oral rinse (Mouthwash): Should be used to reduce bacterial colonization of the mucosa.
 - Enziclor Mouthwash OR Clinica Mouthwash OR Listerine mouthwash
 - Potent topical corticosteroid ointment is recommended during the acute phase of the illness.



- NUTRITIONAL SUPPORT:** Nutritional support should be administered orally if possible. For patients unable to tolerate oral intake, provide enteral feeding through a nasogastric tube. Nasogastric tube placement should be avoided in patients with nasopharyngeal mucosa involvement. Nutritional support of 30-35 kcal/kg should be delivered, maintaining close glycemic control. If the patient's caloric intake is not sufficient with enteral nutrition, it should be supplemented via the parenteral route.
- Supportive treatment of OCULAR involvement:** Ophthalmologic consultation and a full exam upon admission
- » Ocular lubricants should be administered every 2 hours: Tear plus eye drops, Systane eye drops.
 - » Daily exam of the entire ocular surface (eyelid skin & margin, conjunctiva, & cornea) is recommended.
- Supportive treatment of UROGENITAL involvement:** Urogenital involvement occurs in approximately 70% of women and men with SJS/TEN. This can result in erosions of the scrotum/labia, penis/vulva; dysuria; hematuria; urinary retention; and long-term sequelae such as urethral stenosis and scarring, xerosis, phimosis, dyspareunia, chronic pain, bleeding, sexual dysfunction, infertility, and anxiety.
- » Exam of the urogenital tract of all patients with SJS/TEN is recommended upon initial assessment and daily during hospitalization. A urinary catheter should be inserted if urogenital involvement is causing significant dysuria/retention.
 - » The vulvar/urogenital skin/mucosa should be coated with an ointment and/or ointment gauze to help reduce pain and adhesion formation, and facilitate healing, during the acute phase of the disease.
 - » For women with suspected vaginal involvement, an intra-vaginal dilator can be used to apply a petrolatum jelly, with reapplication as frequently as necessary to maintain barrier protection and/or a high-potency corticosteroid ointment if active inflammation is observed. Tapering of the topical corticosteroid use should be based on clinical improvement.
 - » If vaginal candidiasis is suspected, obtain a potassium hydroxide preparation and fungal culture and initiate treatment with a suitable antifungal medication.
 - » Medication can be alternated with estrogen cream to encourage healing of the vaginal mucosa.
 - » Intravaginal dilators can be in place for a maximum of 24 hours before replacement. If patients are not comfortable using an intra-vaginal dilator, medication can be applied with a vaginal applicator.
 - » Menstrual suppression may reduce the risk of vaginal adenosis and endometriosis and can be considered in women with severe genital mucosal involvement.
- Prophylactic systemic antibiotic therapy is not routinely recommended:** Consider only in wound infection or sepsis, empirically treat for MRSA until ruled out with vancomycin; treat for Pseudomonas with cefepime OR Ceftazidime, if suspected.
- IVIG and Cyclosporin may slow progression.**



SUNBURN

Definition: Sunburn is an acute self-limited inflammatory skin reaction that occurs after excessive ultraviolet radiation (UVR) exposure and typically manifests as a first-degree burn. It more commonly affects individuals with light skin than those with darker skin.

Etiology: Sunburn is most commonly caused by ultraviolet B (UVB) radiation.

Risk factors for sunburn

- Individuals who are sensitive to UV radiation, e.g. those with:
 - Light skin tones
 - History of sunburn within 1 hour of exposure to UVR
 - History of photodermatoses
- Non-adherence to photoprotective measures
- Use of indoor tanning beds or tanning products.
- Extensive time spent outdoors for work or recreation.

Pathophysiology: UV radiation → DNA mutations → apoptosis of keratinocytes in the epidermis & release of inflammatory markers (such as chemokines, prostaglandins) → inflammation of the dermis hours after exposure



Clinical features

The following typically manifest 4–12 hours after UVR exposure:

- » Erythema
- » Pruritus
- » Tenderness
- » Swelling
- » Blanching
- » Warmth

Features of severe sunburn may also be present and include:

- » **Systemic symptoms:** Headache, fever, nausea, fatigue, dehydration
- » Weeping, wet skin
- » Blisters with clear fluid

Peak severity is usually 24–36 hours after exposure.

Resolution typically occurs within 3–8 days; characterized by dry, hyperpigmented skin that easily peels.

Diagnosis

Sunburn is a clinical diagnosis based on:

- » Recent history of UVR exposure
- » Clinical features of sunburn

Diagnostic uncertainty: Consider diagnostics for photodermatoses.

Caution

Do not use very cold wet dressings or ice to cool sunburn; ice causes vasoconstriction of blood vessels in the dermis, which can damage the tissue further.

Avoid using moisturizers and cooling ointments on broken skin (open blisters)



General principles of treatment

- ☞ Sunburn is typically managed with supportive therapy in the outpatient setting.
- ☞ **Further sun exposure should be avoided:** Sun avoidance when possible, Protective clothing, Sunscreen
- ☞ Clean, loose cotton clothing can protect the skin while it heals
- ☞ **Sunburn with severe features may require:**
 - » Dressings and topical antiseptic ointment for blisters
 - » Hydrate patient and treat as burns
- ☞ To reduce the risk of recurrence, educate patients on prevention of sunburn.
- ☞ Oatmeal Bath with lukewarm water.
- ☞ Moisturizers (e.g., coconut oil, petroleum jelly, lotions); can be refrigerated before use to increase relief
- ☞ Cooling ointments (e.g., aloe vera)
- ☞ Wet gauze or a cool cloth

Supportive treatment, If symptoms do not improve, consider adding the following:

- » One of the following oral Anti-histamines:
 - ☞ Tab. Cetirizine 10mg (Rigix, Zyrtec)
 - OR Tab. Levocetirizine 5mg (T-day, Belair, Xyzal)
 - OR Tab. Loratidine 10mg (Softin, Lorin NSA, Lormax)
 - Twice daily for allergies/itchy skin (Pruritus)
- » Oral analgesia/NSAIDs for persistent pain:
 - ☞ Tab. Paracetamol 325mg+Tramadol 37.5mg (Distalgesic)
 - OR Tab. Diclofenac sodium 50mg (Voren, Voltal)
 - Twice or three times daily

Topical steroids are widely used to treat sunburn; however, there is a lack of evidence supporting their use.

- » Betamethasone Cream or ointment (Betnovate, Prostate)
- OR Fluticasone Cream or ointment (Cutivate, Tioovate)
- OR Clobetasol Cream or ointment (Clobivate, Dermovate)
- Apply twice daily on affected side

COMMONLY USED DERMATOLOGICAL (SKIN) DRUG BRAND IN PAKISTAN

Hydrocortisone	» Lacticare HC 1% & 2.5% Lotion (Stiefel GSK) » Cortival 1% Cream (Valor Pharma) » Hydrocortisone Cream (ZAFA)
Methylprednisolone	» Advantan Fatty ointment (Bayer) » Advantan Cream (Bayer) » Advacort Cream & Ointment (Atco Pharma) » Solu-Medrol 125mg 500mg & 1g Injection (Pfizer)
Difflocortolone	» Nerisone Forte Ointment
Hydrocortisone + Clotrimazole	» Hydrozole Cream (Stiefel GSK) » Aquazole Cream » Clozox-H Cream (Shaigan) » Curezole Cream (Atco Pharma) » Spectrazole Cream (Pharma Health)
Hydrocortisone + Clotrimazole + Gentamycin	» Spectrazole-G Cream (Pharma Health)
Betamethasone	» Tab. Betnelar 0.5mg (GSK) » Tab. Betnesol 0.5mg (GSK) » Inj. Betnesol 4mg (GSK) » Betnovate Ointment & Cream (GSK) » Betaderm Ointment, Cream & Lotion (Atco Pharma) » Provate Cream & Lotion (Saffron Pharma) » Effidex lotion & Ointment (Pharma health)
Betamethasone + Salicylic acid	» Provate-S Ointment & Lotion (Saffron Pharma) » Betasalic Ointment & Lotion (Atco Pharma) » Novasalic Ointment & Lotion (Pharma Health)
Betamethasone + Neomycin	» Betnovate N Ointment, Cream & Lotion (GSK) » Betaderm N Ointment & Cream (Atco Pharma)
Betamethasone + Neomycin + Miconazole	» Betaderm NM Cream (Atco Pharma)
Miconazole + Gentamicin + Betamethasone	» Micogen-B Cream (Valor Pharma) » Mycona GB Cream (Valor Pharma)
Miconazole	» Mycon 2% Cream (Valor Pharma) » Daktarin 2% Cream (Aspin Pharma) » Daktarin Oral Gel Cream (Aspin Pharma) » Macnaz Gel (Opal Pharma)
Miconazole + Gentamicin	» Mecona Cream (Valor Pharma)
Miconazole + Hydrocortisone	» Daktacort Cream (Aspin Pharma) » Mycon-H Cream (Valor Pharma)
Betamethasone + Gentamicin	» Betagenic Ointment & Cream (Atco Pharma) » Provate-G Cream (Saffron Pharma) » Effigenta Ointment & Cream (Pharma Health)
Clobetasol	» Dermovate Ointment & Cream (GSK) » Clobevate Ointment & Cream (Stiefel GSK) » Clobederm Ointment, Cream & Lotion (Atco Pharma)
Clobetasol + Salicylic acid	» Clobederm-S Lotion (Atco Pharma)
Clobetasol + neomycin + nystatin	» Dermovate Ointment NN (GSK) » Clobederm NN Ointment (Atco)
Azelaic acid	» Skinoren Cream (Bayer)
Tacrolimus	» Imunol Ointment (Saffron Pharma) » Eczemus Ointment (Saffron Pharma)

Fluticasone	» Crolimus Ointment
Mometasone	» Cutivate Ointment & Cream (GSK)
Mupirocin	» Ticovate Cream & Lotion (Saffron Pharma)
	» Hivate Cream & Lotion (Saffron Pharma)
	» Santomet Cream & Lotion (Sante Pharma)
	» Bactroban Ointment & Cream (GSK)
	» Mupir Ointment (Valor Pharma)
Lidocaine	» Xylocaine 2% Jelly (BARRETT HODGSON)
	» Xyloaid 2% Jelly (BARRETT HODGSON)
	» Xyloaid 5% Ointment (BARRETT HODGSON)
	» Xylocaine 5% Ointment (BARRETT HODGSON)
	» Xylocaine 2%/10ml Injection
	» Xylocaine 4%/50ml Topical Solution
Fluticasone + Mupirocin	» Cutivate-M Ointment (GSK)
Triamcinolone + Nystatin + Neomycin + Gramicidin	» Kenacomb Ointment (GSK)
	» Kenacomb Cream (GSK)
Minocycline + Bacitracin + Lidocaine + Polymyxin B	» Polyfax Plus (GSK)
Bacitracin + Polymyxin B	» Polyfax Skin (GSK)
Clindamycin	» Clinagel 1% Gel (Stiefel GSK)
	» Acsolve 1% Gel & Lotion (Atco Pharma)
	» Cap. Dalacin-C 150mg & 300mg (Pfizer)
	» Inj. Dalacin-C 300mg & 600mg (Pfizer)
	» Dalacin T Lotion (Pfizer)
	» Clycin T Lotion (Shaigan Pharma)
Benzoyl peroxide	» Brevoxyl Cream (Stiefel GSK)
	» Panoxyl-5% & 10% Gel (GSK)
	» Panoxyl-5% Bar (GSK)
	» Benzacide Bar 5% (Pharma Health)
Benzoyl peroxide + Clindamycin	» Duac gel (Stiefel GSK)
	» Benclin Gel (Sante Pharma)
	» Dupearl Gel
	» Clinda Plus Gel
Benzoyl Peroxide 2.5% + Adapalene 0.1%	» Acne-Pearl Plus Gel
	» Adarex gel
	» Differin gel
Lactic acid + Salicylic acid	» Duofilm Lotion (Stiefel GSK)
dl-lactic acid + pidolic acid	» Lacticare Lotion (Stiefel GSK)
Tretinoin 0.05%	» Retin-A
	» Skin-A Cream (Atco Pharma)
	» Tretinex Cream (Dermagen)
Clindamycin + Tretinoin	» Cleret Gel (Tabros Pharma)
	» Acdermin Gel (Atco Pharma)
	» Clinda-T Gel (Valor Pharma)
Hydroquinone	» Hyderquin 2% and 4% Cream (Atco Pharma)
	» Safoquin 2% and 4% Cream (Saffron Pharma)
Hydroquinone + Glycolic Acid	» Sanclear Cream (Sante Pharma)
Clioquinol	» Clioquinol 3% (zafa Pharma)
Fluocinolone	» Synalar Gel (Pharma health)
Fluocinolone + Neomycin	» Synalar-N Cream (Pharma health)
Fluocinolone + Clioquinol	» Synalar-C Cream (Pharma health)
	» Hyderquin Plus Cream (Atco Pharma)

Fluocinolone + Hydroquinone + Tretinoin	» Retrieve Cream (Pharma health) » Siton-Plus Cream (Shaigan Pharma) » Flytro Cream (Tabros Pharma) » Tri-Melasin Cream » Lazma Cream
Isotretinoin	» Isotrex Gel (Stiefel GSK) » Isotin Gel (Shaigan Pharma) » Cosmin Gel (Saffron Pharma) » Cap. Accutane 20mg (Pharma health) » Cap. Arynoin 10 & 20mg (Pharma health) » Cap. Isozam 10mg & 20mg (Valor/Leo Pharma) » Cap. Maxinoin 10mg & 20mg (Maxitech)
Erythromycin + Isotretinoin	» Isotrexin Gel (Stiefel GSK) » Arynoin Plus Gel (Pharma health) » Erynocin Gel (Sante Pharma) » Clarixin gel
Adapalene	» Adapco Gel & Cream (Atco Pharma) » Clear Cream (Saffron Pharma) » Gallet gel
Glutathione	» Inj. Tationil 600mg/4ml » Cap. Glutamax 500mg » Glutamax cream
Lindane 1%	» Lice-O-Nil Cream (Wilson Pharma) » Vandan Lotion (Valor Pharma)
Permethrin 5%	» Lotrix Lotion & Cream (GSK) » Scabfree Lotion & Cream (Atco Pharma) » Mitonil Lotion & Cream (Saffron Pharma)
Crotamiton	» Cortan cream
Crotamiton + sulphur	» Scabion Lotion (Atco Pharma) » Scabion Forte Lotion (Atco Pharma) » Scabion Cream (Atco Pharma)
Eflornithine hydrochloride (For the reduction of unwanted facial hair growth in women)	» Depilus Cream (Atco Pharma) » Vanifall Cream (Brooks Pharma) » Santhine Cream (Sante Pharma)
Minoxidil 5% solution or foam (50mg/60ml)	» Rogaine 5% (=50mg/ml) solution and Rogaine 5% foam » Minoxin Plus 5% solution » Hairmax Plus 5% solution
Minoxidil 2% solution or foam (20mg/60ml)	» Rogaine 2% (=20mg/ml) solution and Rogaine 2% foam » Minoxin 2% solution » Hairmax 2% solution
Procapil (With Isochrysis Galbana Extract)	» Piligrow Plus 5% solution (Hairspray) » Piligrow Plus 2.5% solution (Hairspray)
Procapil + Anagain hair spray	» Reegain Hair Spray
Anthralin 0.5%	» Dithroderm 0.5% cream
Lidocaine + Neomycin + Polymyxin + Bacitracin	» Healt Skin Ointment (Atco Pharma)
Bufexamac + Neomycin + Nystatin	» Flogocid Cream » Bufac Cream
Fusidic Acid	» Fucidin Cream (Leo Pharma) » Fusiderm Ointment & Cream (Martin Dow) » Fusil Cream (Tabros Pharma) » Fusiderm 350

Fusidic Acid + Hydrocortisone	» Fucidin 250mg Tablets (Leo Pharma)
	» Fucidin-H Cream (Leo Pharma)
	» Fusiderm-H Cream (Martin Dow)
	» Fusil-HC Cream (Tabros Pharma)
Fusidic Acid + Betamethasone	» Fusil-B Cream (Tabros Pharma)
	» Fucort-B Cream (Saffron Pharma)
	» Fucicort (Leo Pharma)
Calcipotriol	» Daivonex 50mcg Ointment (Leo Pharma)
Calcipotriol + Betamethasone	» Daivobet 50mcg Ointment (Leo Pharma)
Isoconazole	» Travogen Cream (Bayer)
Isoconazole + Diflucortolone	» Travocort Cream (Bayer)
Clotrimazole	» Canesten Cream (Bayer)
	» Stiemazole Cream & Lotion (Stiefel GSK)
	» Clotrim Cream & Lotion (Zafa Pharma)
	» Dermosporin Cream & Lotion (NQ Pharma)
Bifonazole 1%	» Canesten Extra Cream (Bayer)
	» Bifomyk Cream
Dexamethasone + Clotrimazole	» Baycuten-N Cream (Bayer)
Dexamethasone + Neomycin	» Kanadex-N Cream (ISIS Pharma)
	» Dexamin-N Cream (Geofman Pharma)
Dexpanthenol (Nappy Rash)	» Bepanthen Ointment (Bayer)
Zinc Oxide + Benzalkonium	» Rashnil Cream (ABBOTT)
Euflavine	» Burnol Cream (ABBOTT)
Silver Sulphadiazine 1%	» Dermazin Cream (NOVARTIS)
	» Quench Cream (FEROZSONS)
Ivermectin	» Tab Ivermite 6mg (Atco Pharma)
	» Tab Mectimite 6mg (Pharma Health)
Terbinafine	» Terbisil Cream & Lotion (Saffron)
	» Tab. Terbisil 125mg & 250mg (Saffron)
	» Terbiderm Cream & Lotion (Atco)
	» Tab. Terbiderm 125mg & 250mg (Atco)
Acitretin	» Cap. Tigasor 10mg & 25mg (Maxitech)
	» Cap. Neotret 10mg & 25mg Pharma Health)
	» Tab. Zovirax 200mg,
	» Zovirox 5% cream (GSK)
	» Tab. Acylex 200mg, 400mg & 800mg (FEROZSONS)
	» Acylex 5% cream
	» Syp Acylex 200mg/60ml
	» Tab. Cycloz 200mg, 400mg and 800mg (Highnoon)
	» Syp. Cycloz 200mg/60ml
	» Cycloz 5% cream
	» Inj. Cycloz 250mg/vial (Highnoon)
	» Inj. Acyclovir 500mg/10ml vial (ABBOTT)
	» Inj. Aclovir 250mg/10ml vial & 500mg/10ml vial
Acyclovir	» Cap. Diflucan 50mg, 150mg & 200mg (Pfizer)
	» Inj. Diflucan 2mg/ml (50ml) IV Infusion (Pfizer)
	» Cap. Fungone 150mg (Sami Pharma)
	» Cap. Candizol 50mg, 150mg & 200mg (Genetics)
	» Cap. Derocon 50mg & 150mg
	» Syp. Derocon 50mg/5ml (35ml)
Fluconazole	

Ketoconazole	» Conaz 20mg/60ml Lotion 'Shampoo'
	» Conaz 2% Cream
	» Tab. Conaz 200mg (Atco)
	» Nizoral 2% Cream & Nizoral Lotion (Aspin Pharma)
	» Cap. Nizoral 200mg
	» Ketonaz 2% Lotion (Sante Pharma)
	» Ketowin 2% Lotion (Shaigan Pharma)
	» Tab. Tezole 200mg (Brookes) » Tezole 2% Cream (Brookes)
Itraconazole	» Cap. Icon 100mg (FEROZSONS)
	» Cap. Rolac 100mg (Sami Pharma)
	» Cap. Sporanox 100mg (Aspin Pharma)
Voriconazole	» Tab. Vorif 50mg, & Tab. Vorif 200mg (FEROZSONS)
	» Tab. Voricon 50mg, & Tab. Voricon 200mg
	» Inj. Vorix 200mg
Posaconazole	» Tab. Noxafil 100mg
	» Syp. Noxafil 50mg/ml
	» Inj. Noxafil 300mg/16.7ml (18MG/ml)
Oxiconazole nitrate	» Xirconi 1% Cream
Griseofulvin	» Tab. Grisovin 500mg
	» Tab. Grifin 500mg
	» Tab. Graso-F 500mg
	» Tab. Fungivin 500mg
Amphotericin B	» Inj. Amphotret 50mg/vial
	» Inj. Fungizone 50mg/vial
	» Inj. Anfotericina Fada 50mg/vial
	» Inj. AmBisome 50mg/vial (Liposomal Amphotericin B)
Caspofungin	» Inj. Cansidas 50mg/vial & Inj. Cansidas 70mg/vial
	» Inj. Casfung 50mg/vial & Inj. Casfung 70mg/vial
Prednisolone	» Tab. Deltacortril 5mg (Pfizer)
	» Tab. Rapicort 5mg (Tabros Pharma)
	» Syp. Rapicort 15mg/5ml (Tabros Pharma)
	» Syp. Steron 15mg/5ml (Xenon Pharma)
Triamcinolone acetonide	» Inj. K-Cort 40mg/1ml (Ophth Pharma)
	» Inj. Lonacort 40mg/1ml (ZAFA)
	» Inj. Kenacort-A 40mg/1ml (GSK)
	» Kenalog in orabase 1% ointment
	» Triton 1% ointment, Inj. Triton 40mg/ml
Dexamethasone	» Tab. Kanadex 5mg (ISIS Pharma)
	» Inj. Decadron 4mg/1ml, Inj. Decadron 4mg/5ml
Minocycline	» Inj. Dexamethasone 4mg/1ml (Amros Pharma)
	» Tab. Minoderm 100mg (Stiefel GSK)
	» Tab. Minogen 100mg (Pharma Health)
Doxycycline	» Cap. Vibramycin 100mg (Pfizer)
	» Cap. Doxyn 100mg (Sami Pharma)
	» Cap. Wellcodox 100mg (GSK)
	» Tab. Adoxa 100mg (Pharma Health)
Azithromycin	» Cap. Azomax 250mg
	» Tab. Azomax 500mg
	» Cap. Macrobac 250mg
	» Tab. Macrobac 500mg

	» Cap. Zetro 250mg » Tab. Zetro 250mg & Tab. Zetro 500mg » Syrup 200mg/5ml: Syp. Azomax, Syp. Zetro, Syp. Plazo
Pheniramine maleate	» Tab. Avil 25mg (Sanofi Aventis)
Hydroxyzine	» Syp. Avil 15mg/5ml, Inj. Avil 50mg/2ml
Clemastine	» Tab. Atarax 10mg & 25mg (GSK)
	» Tab. Tandegyl 1mg & 2mg
	» Tab. Klemat 1mg & 2mg
Cetirizine	» Tab. Rigix 10mg, Syp. Rigix 5mg/5ml » Tab. Zyrtec 10mg, Syp. Zyrtec 5mg/5ml » Tab. Baydal 10mg, Syp. Baydal 5mg/5ml
Levocetirizine	» Tab. Belair 5mg » Tab. Xyzal 5mg » Tab. Leozin 5mg » Tab. T-day 5mg 5ml, Syp. T-day 2.5mg/5ml » Tab. Neo-Sedil 5mg, Syp. Neo-Sedil 2.5mg/5ml
Ebastine	» Tab. Kestine 10mg & 20mg (Highnoon) » Syp. Kestine 5mg (Highnoon)
Loratidine	» Tab. Lorin NSA 10mg, Syp. Lorin NSA 5mg/5ml » Tab. Softin 10mg, Syp. Softin 5mg/5ml
Desloratadine	» Tab. Destina 5mg (Hilton) » Tab. Larinex 5mg (Getz) » Tab. Neo-Antial 5mg, Syp. Neo-Antial (Sami) » Tab. Jordin-D 5mg, Syp. Jordin-D (HIGH-Q)
Fexofenadine	» Tab. Telfast 60mg, 120mg & 180mg (GSK) » Tab. Fexet 60mg, 120mg & 180mg (GSK) » Tab. Fexo 60mg, 120mg & 180mg (GSK)
Methoxsalen	» Tab. Lukodermine 10mg » Lukodermine 1.00% ointment
Methotrexate	» Tab. Unitrexate 2.5mg & Tab. Unitrexate 10mg » Inj. Unitrexate 50mg/2ml vial » Tab. Cytotrexate 2.5mg & Tab. Cytotrexate 10mg » Inj. Methotrexate 50mg/2ml vial (PARKE DEVIS) » Inj. Zexate 500mg/20ml vial
Azathioprine	» Tab. Imuran 50mg » Tab. Amarin 50mg » Tab. Azafrine 50mg
Cyclosporin	» Tab. Sandimmun Neoral 25mg » Tab. Sandimmun Neoral 100mg » Syp. Sandimmun Neoral-D 100mg/ml (50ml) » Tab. Cypol-N 50mg » Tab. Cypol-N 100mg » Tab. Bioral 50mg » Tab. Bioral 100mg
Mycophenolate Mofetil	» Tab. Cycopin 250mg » Tab. Myfortic 360mg » Tab. Mygraf 500mg » Tab. Cellcept 500mg » Tab. Mycolate 500mg





APPROACH TO THE MANAGEMENT OF ACUTE ABDOMEN

➤ Start with Presenting complaint and history of presenting complaint

Make your approach in a case of acute abdomen as following:

1. **Onset:** When did the chief complaint occur (gradual, rapid or sudden, intermittent or constant)
2. **Duration:** When do the symptoms occur? At night, all the time, in the mornings, etc..
3. **Progression:** Is this problem getting worse or better Is there anything that the patient does that makes it better or worse
4. **Aggravating factor:**
5. **Radiation:** Do the symptoms radiate to anywhere in the body, and if so, where? Pain in left chest radiating to left arm is which suggestive of ischemic heart disease. Pain in flanks radiating to groins is feature of ureteric (stone) pain
6. **Relieving factors:** Relie f with food, Position...
7. **Scale:** On a scale of 1 to 10, how bad are the symptoms
8. **Site:** Anatomical location, or region
9. **Associated symptoms:** any other info about the chief complaint that has not already been covered
Ask if there is anything else that the patient has to tell about the chief complaint. (Nausea, Vomiting);
Vomiting: It can occur in acute abdominal but remains persistent in upper intestinal obstruction)

Ask about:

- » **Systemic signs and symptoms:** fever, jaundice, loss of weight or anorexia, effect on everyday life.
- » **Upper gastrointestinal (GI) signs and symptoms:** dysphagia, indigestion (heartburn), nausea, vomiting, haematemesis.
- » **Lower GI signs and symptoms:** diarrhoea or constipation, melaena or rectal bleeding, Steatorrhea.
- » **Genitourinary signs and symptoms:** frequency, dysuria, haematuria.
- » **Gynaecological signs and symptoms:** length of menstrual period, amount of bleeding, pain, Intramenstrual bleeding, last menstrual period.

Complete detail about Past medical history, Drug history, Family history, social history

What is the character of pain?

Pain can be of following character	
» Burning	» Stabbing or crushing
» Gripping heaviness	» Pricking
» Dull	» Colicky
» Throbbing	»

➤ Start GPE and whole abdomen examination.

❖ **Gesture of Patient:** Particular gestures useful in analyzing specific pain symptoms

» A squeezing gesture to describe cardiac pain
» Hand position to describe renal colic
» Rubbing the sternum to describe heartburn
» Rubbing the buttock and thigh to describe sciatica
» Arms clenched around the abdomen to describe mid-gut colic



► FIRST RULE OUT THE ETIOLOGY

1. Acute coronary syndrome

- » Heavy, dull, pressure/squeezing sensation
- » Substernal or epigastric pain with radiation to left shoulder
- » Nausea, vomiting
- » Diaphoresis, anxiety
- » Dizziness, lightheadedness, syncope
- » Pain may improve with nitroglycerin.
- » **Diagnostic findings:**
 - **ECG:** nonspecific changes, ST-segment elevation/depression, T-wave inversions, Q waves
 - **Lab:** Increased or normal troponin
 - **Transthoracic Echocardiography (TTE):** hypokinesis, regional wall motion abnormalities

2. Acute mesenteric ischemia

- » Age > 60 yrs, embolic risk factors (e.g., atrial fibrillation, thrombophilia), cardiovascular disease
- » Pain out of proportion to findings
- » Severe, diffuse abdominal pain and distention
- » Vomiting, diarrhea
- » Melena, Hematechezia
- » **Diagnostic findings:**
 - **Labs:** lactic acidosis, hyperkalemia, leukocytosis
 - **X-ray abdomen:** normal (early stages), pneumatosis intestinalis (late stages)
 - **CT angiography:** mesenteric arterial narrowing or occlusion, thickening of bowel wall, nonenhancing segments of solid organs or of the bowel wall, pneumatosis intestinalis

3. Rupture or impending rupture of Abdominal aortic aneurysm (AAA):

- » Age > 50 years
- » Sudden, severe central abdominal, chest, and/or back pain
- » Hypotension, shock
- » Pulsatile mass in the midline of the abdomen
- » Grey Turner sign and/or Cullen sign
- » History of atherosclerosis, hypertension, and/or smoking
- » **Diagnostic findings:** Imaging is only recommended in hemodynamically-stable patients with a low pretest probability of ruptured AAA.
 - **Ultrasound Abdomen:** aortic dilatation, periaortic fluid, intraperitoneal free fluid
 - **CT scan/MR angiography:** retro- and intraperitoneal hemorrhage; localization of the ruptured/leaking site

4. GI perforation and Peritonitis:

- » Sudden onset of diffuse abdominal pain
- » Nausea, vomiting
- » Constipation/obstipation
- » Diffuse abdominal guarding, rigidity, and rebound tenderness
- » Absent bowel sounds
- » Loss of liver dullness on RUQ percussion
- » **Diagnostic findings:**
 - **Abdominal x-ray:** pneumoperitoneum



5. Aortic dissection

- » Sudden onset of severe, sharp tearing chest or abdominal pain that radiates to the back
- » Hypotension, syncope, neurological symptoms
- » Asymmetrical blood pressure, pulse deficit
- » New diastolic murmur (due to aortic regurgitation)
- » Symptoms of myocardial ischemia
- » **Diagnostic findings:**
 - **D-dimer:** Elevated
 - **ECG:** nonspecific ST-segment changes
 - **CXR:** widening of the aorta
 - **CT angiography of chest/abdomen/pelvis:** intimal flap with false lumen
 - **Echocardiography:** proximal aortic dissection, tamponade, aortic regurgitation

6. Acute Appendicitis:

- » Pain in right iliac fossa, epigastric, and/or periumbilical pain (migrating abdominal pain)
- » Fever, Nausea, anorexia
- » Guarding, tenderness, and rebound tenderness in the right lower quadrants (RLQ)
- » McBurney's sign positive
- » **Diagnostic findings:**
 - **CBC:** Neutrophilic leukocytosis
 - **CT Abdomen with IV contrast:** distended appendix with periappendiceal fat stranding
 - **Ultrasound Abdominal:** noncompressible, aperistaltic, distended appendix, probe tenderness in the right lower quadrants (RLQ), Target sign

7. Mechanical bowel obstruction

- » Colicky abdominal pain
- » Obstipation/bloating
- » Progressive nausea and vomiting (late finding)
- » Diffuse abdominal distention, tympanic abdomen, collapsed rectum on DRE
- » Tinkling bowel sounds
- » History of abdominal surgery
- » **Diagnostic findings:**
 - **X-ray abdomen:** Dilated bowel loops proximal to the obstruction, Rectal air shadow absent, Multiple air-fluid levels
 - **CT abdomen with IV and oral contrast:** Similar findings as on x-ray, Transition point at site of obstruction

8. Peptic ulcer disease:

- » Epigastric pain
- » **Duodenal ulcer:** pain relieved with food; weight gain
- » **Gastric ulcer:** pain exacerbated by food; weight loss
- » Signs of gastrointestinal (GI) bleed
- » History of NSAID intake
- » **Diagnostic findings:**
 - CBC shows Anemia
 - Positive Fecal occult blood test (in cases of bleeding ulcer)
 - **Urea breath test for H. pylori:** positive in most cases of PUD
 - **Esophagogastroduodenoscopy (EGD):** Mucosal erosions and/or ulcers are required for a



9. Acute pancreatitis

- » Severe epigastric pain that radiates to the back (circumferential pain)
- » Nausea, vomiting
- » Epigastric tenderness, guarding, rigidity
- » Hypoactive bowel sounds
- » Possibly fever
- » History of gallstones or alcohol use
- » **Diagnostic findings:**
 - Elevated Lipase and amylase
 - Hypocalcemia (poor prognostic indicator)
 - **Ultrasound Abdomen:** pancreatic edema, peripancreatic fluid, gallstones
 - **CT Abdomen with IV contrast:** pancreatic edema, peripancreatic fat stranding, gallstones

10. Symptomatic cholelithiasis

- » **Biliary colic:** RUQ pain with radiation to the right shoulder
- » Postprandial onset
- » Nausea, vomiting
- » Normal abdominal examination
- » **Diagnostic findings:**
 - **Labs:** maybe normal
 - **Ultrasound Abdomen:** gallstones with posterior acoustic shadow

11. Choledocholithiasis

- » Right upper quadrants (RUQ) pain
- » Features of obstructive jaundice
- » Nausea, vomiting
- » Normal abdominal examination
- » **Diagnostic findings:**
 - **Labs:** Elevated ALP, AST, ALT and total bilirubin
 - **Ultrasound Abdomen:**
 - ✓ Dilated common bile duct (CBD)
 - ✓ Intrahepatic biliary dilatation
 - ✓ Echogenic structure within the CBD with shadowing
 - **MRCP or ERCP:** filling defect in the contrast-enhanced duct

12. Acute cholecystitis

- » Severe right upper quadrants (RUQ) pain
- » Fever, chills, Nausea, vomiting
- » Right shoulder referred pain
- » **Murphy sign**
- » **Diagnostic findings:**
 - **CBC:** Raised WBC
 - **Ultrasound abdomen:** sonographic Murphy sign, pericholecystic fluid collection, gallbladder wall thickening, and/or edema (double-wall sign)
 - **HIDA scan:** nonvisualization of the gallbladder



13. Acute cholangitis

- » **Charcot triad:** Right upper quadrant (RUQ) pain, fever, and jaundice
- » **Reynold pentad:** Charcot triad + hypotension and mental status changes
- » **Diagnostic findings:**
 - **Laboratory findings:**
 - ✓ Raised WBC and raised CRP
 - ✓ Elevated ALP, AST, ALT, GGT and Total bilirubin
 - ✓ Positive blood cultures
 - **Right upper quadrant (RUQ) ultrasound:** biliary dilation and/or evidence of obstruction (e.g., choledocholithiasis), thickening of bile duct walls
 - **MRCP/ERCP:** findings similar to those on ultrasound

14. Diverticulitis:

- » Fever
- » Lower left quadrant (LLQ) pain
- » Constipation
- » Tender mass in lower left quadrant
- » **Diagnostic findings:**
 - **CBC:** Raised WBC
 - **CT abdomen with IV and oral contrast:** colonic diverticula with pericolic mesenteric fat stranding

15. Ruptured ectopic pregnancy

- » Sudden severe lower abdominal pain
- » Vaginal bleeding or amenorrhea
- » Lower abdominal guarding and tenderness
- » Cervical motion tenderness, closed cervix
- » Enlarged uterus
- » Tachycardia, hypotension
- » **Diagnostic findings:**
 - Elevated Beta-hCG level
 - **Ultrasound Transabdominal/transvaginal**
 - ✓ Free fluid within Morison pouch and/or pouch of Douglas
 - ✓ Empty uterine cavity, thickened endometrial lining
 - ✓ Adnexal mass
 - ✓ Tubal ring sign

16. Ovarian torsion

- » Sudden onset unilateral lower abdominal or pelvic pain
- » Nausea, vomiting
- » Unilateral iliac fossa tenderness
- » **Diagnostic findings:**
 - **Pelvic (or transvaginal) ultrasound with Doppler velocimetry:** enlarged, edematous ovaries with decreased blood flow
 - **Pelvic CT scan with IV contrast**
 - ✓ Unilateral thickened ovarian tube, enlarged ipsilateral ovary, and decreased enhancement of ipsilateral ovary
 - ✓ Twisted mesovarium (whirlpool sign)



17. Testicular torsion

- » Severe lower quadrant and testicular pain
- » Nausea and vomiting
- » Abnormally elevated position of the testis within the scrotum
- » **Diagnostic findings:**
 - **Clinical diagnosis**
 - **Doppler ultrasound:** twisting of the spermatic cord; reduced perfusion of the affected testicle

18. Acute pyelonephritis

- » High fever, chills
- » Flank pain with costovertebral angle tenderness (usually unilateral, may be bilateral)
- » Dysuria, urinary frequency, urgency
- » **Diagnostic findings:**
 - **Labs**
 - ✓ Raised WBC, CRP and ESR
 - ✓ Positive urinalysis
 - ✓ Positive urine culture
 - **US KUB:** edema and focal hypoechogenic areas
 - **CT pelvis with IV contrast:** focal area(s) of hypoenhancement that extend to the cortical periphery

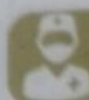
19. Nephrolithiasis

- » Severe unilateral and colicky flank pain (renal colic)
- » Hematuria
- » Nausea, vomiting
- » Dysuria, frequency, and urgency
- » **Diagnostic findings:**
 - **Urine dipstick and urinalysis:** gross or microscopic hematuria
 - **Urine microscopy:** to detect crystals
 - **Abdomino-pelvic CT:** Non-enhanced CT scan is the gold standard.
 - **Ultrasound:** method of choice for patients in whom radiation exposure should be minimized (e.g., pregnant patients, children, recurrent stone formers)



DIFFERENTIAL DIAGNOSIS AND CAUSES OF ACUTE ABDOMEN

Location	Gastrointestinal causes	Nongastrointestinal causes
RUQ	» Biliary colic » Acute cholecystitis » Acute cholangitis » Emphysematous cholecystitis » Acute hepatitis » Pyogenic liver abscess » Duodenal ulcer » Portal vein thrombosis	» Lower lobe pneumonia » Lower lobe pulmonary infarction (pulmonary embolism) » Empyema » Ureteric colic » Pyelonephritis
LUQ	» Gastric ulcer » Splenic abscess » Splenic laceration » Splenic infarction	
RLQ	» Acute appendicitis » Colitis » IBD	» Ureteric colic (nephrolithiasis) » Ectopic pregnancy » Ovarian torsion » Ruptured ovarian cyst » PID » Testicular torsion
LLQ	» Diverticulitis » Colitis » IBD	
Epigastrium	» Acute Esophagitis » Acute Gastritis » Acute Pancreatitis » Acute Mesenteric Ischemia » PUD » GERD » Functional Dyspepsia » Mallory Weiss syndrome	» Myocardial infarction » Pericarditis » AAA » Aortic dissection
Periumbilical	» Acute appendicitis (early) » Mesenteric ischemia	» AAA » Aortic dissection
Suprapubic	» Diverticulitis	» Ectopic pregnancy » PID » Cystitis (UTI) » Prostatitis
Diffuse abdominal pain	» Bowel obstruction » Bowel perforation (peritonitis) » Mesenteric ischemia (peritonitis) » Retroperitoneal hematoma » Constipation » Gastroenteritis » Spontaneous bacterial peritonitis	» Diabetic ketoacidosis » Sickle cell crisis » Porphyria » Cocaine use » Opioid withdrawal » Acute adrenal insufficiency » Irritable bowel syndrome » Heavy metal poisoning



DIAGNOSTIC APPROACH OF ACUTE ABDOMEN:

The diagnostic workup should be guided by the pretest probability of the diagnoses under consideration. The following list includes some commonly used diagnostic tools that can help to diagnose or rule out possible etiologies in a patient with acute abdominal pain.

☛ **Radiological:** The initial imaging modality should be guided by the working diagnosis, as based on the patient history, vital signs, and examination.

A. X-ray Abdomen:

In erect and supine position:

- ☛ Gas under the diaphragm (Due to gut perforation).
- ☛ Dilated loops of bowel or fluid level (Due to intestinal obstruction).

B. **Ultrasound abdomen to rule out:** Gallstone (cholelithiasis), cholecystitis, Pancreatitis, splenomegaly, liver abscess, Hydronephrosis, Kidney stones, appendicitis.

C. CT scan/MRI scan

☛ Laboratory investigation

- ☛ CBC and Serum glucose
- ☛ LFTs, PT INR
- ☛ Urea creatinine and electrolytes.
- ☛ Serum amylase and lipase
- ☛ **Female:** Urine pregnancy test / β -hCG urine test
- ☛ Blood gas analysis (ABGs)
- ☛ Lactate, CRP, ESR
- ☛ Troponin
- ☛ **Culture test:** Blood, Stool, urine
- ☛ Urine analysis

➤ If patient with suspect pancreatitis:

- Pain epigastric with tenderness
- Not relief by ordinary treatment
- Perform serum amylase (most sensitive), serum Lipase (most specific)

➤ If the patient is middle aged → Perform ECG to rule out: MI/Angina/ACS

➤ Then go for murphy sign to exclude cholecystitis

➤ Then rule out:

- **Cystitis and UTI:** by burning sensation, micturition, Suprapubic tenderness/pain
- **Pyelonephritis:** by abdominal pain, fever and renal angle tenderness, WBC

➤ Check urine analysis for Glucose and ketone to rule out DKA

➤ If female patient with lower abdominal pain

▪ Ectopic pregnancy: (classic triad for ectopic pregnancy)

1. Amenorrhea
2. Vaginal bleeding
3. Abdominal pain

▪ Pelvic inflammatory disease (PID):

1. Lower abdominal pain in sexually active women
2. Vaginal discharge

➤ Then look for PUD:

Clinical features + history of drugs Stool test for H.Pylori +ve → treat with Triple therapy

N.B. FEVER + PAIN ABDOMIN:

✓ Never think about Peptic ulcer diseases

✓ Always think about infective cause: Cholecystitis, Liver abscess, Pyelonephritis, Pancreatitis



Radiological Approach of Acute Abdomen

- » The initial imaging modality should be guided by the working diagnosis, as based on the patient history, vital signs, and examination.
- » The following recommendations apply to nonpregnant adults.
- » In pregnant women with acute abdominal pain, ultrasound and/or MRI of the abdomen and/or pelvis without contrast are the preferred initial imaging modalities.

Suspected diagnosis	Recommended imaging modality
Acute coronary syndrome	» ECG, Echocardiography (Transthoracic)
Hemorrhagic shock	» FAST scan
Bowel perforation	» Ultrasound Abdomen & Pelvis » X-ray abdomen (upright and supine) with x-ray chest (upright) » CT abdomen and pelvis with IV contrast
Intra-abdominal abscess	» Ultrasound Abdomen & Pelvis » CT abdomen and pelvis with IV contrast
Acute diverticulitis	
Acute appendicitis	
Acute mesenteric ischemia	» CTA of the abdomen
Acute pancreatitis	» Ultrasound abdomen » CT abdomen with IV contrast
Nephrolithiasis	» Ultrasound abdomen and pelvis/KUB » CT abdomen and pelvis without contrast
Acute complicated pyelonephritis	» CT abdomen and pelvis with IV contrast
Suspected symptomatic Abdominal Aortic Aneurysm in a hemodynamically stable patient	» Ultrasound abdomen » CT/MR angiography
Pelvic pain	» Gynecological etiology suspected: Ultrasound pelvis (transabdominal and/or transvaginal) » Non-gynecological etiology suspected and β-HCG is negative: CT abdomen and pelvis with IV contrast » Suspected ovarian torsion: Duplex ultrasonography of pelvic adnexa » MRI pelvis (+/- abdomen) with IV contrast
Non-localized pain	» CT abdomen and pelvis without IV contrast » MRI abdomen and pelvis with/without IV contrast » Ultrasound abdomen and/or pelvis » Postoperative patients with acute abdomen: consider fluoroscopy (enema and/or upper abdominal series)

RED FLAGS FOR ABDOMINAL PAIN

1. Sudden onset of severe pain
2. Pain that interrupts sleep
3. Bilious vomiting
4. Hematemesis, hemochezia
5. Hypotension, tachycardia
6. Patient lying very still
7. Patient writhing in pain
8. Jaundice
9. Guarding and/or rigidity (focal or diffused)
10. Rebound tenderness (focal or diffused)
11. Absent or tinkling bowel sounds
12. Gross abdominal distention
13. Pain out of proportion to abdominal findings
14. High-risk patient characteristics
 - » Age > 50 years
 - » Previous abdominal surgery
 - » History of CAD and/or atrial fibrillation

Immediately life-threatening diagnoses

1. Ruptured or expanding aortic aneurysm
2. Aortic dissection
3. Myocardial infarction
4. Bowel perforation
5. Mechanical bowel obstruction
6. Acute mesenteric ischemia
7. Acute pancreatitis
8. Acute cholangitis
9. Ruptured ectopic pregnancy



STEPWISE MANAGEMENT OF ACUTE ABDOMEN

Rx

- Maintain ABCD&E
- NPO patient
- IV access with two large-bore IV line
- **IV fluid resuscitation:** Ringer lactate, Normal saline 0.9%, Dextrose 5%
- Hemodynamic and respiratory support
- Consider **Inj. Haemaccel 500ml** x IV x SOS (hypotension/shock)
- Nasogastric tube (NG) placement and Foleys catheterization
- **Vitals monitoring:** Check BP, PR, RR, Temperature, SpO₂ and bed side RBS
- **Send labs:** CBC, Urea, creatinine and electrolytes, LFTs, PT INR and ABGs
- Perform a focused history and physical examination.
- Perform targeted diagnostics and further tests as required.
- Early surgical consult
- Administer supportive care as needed.
- **IV Pain management/analgesia:**
 - ✎ **Inj. Ketorolac 30mg/ml** (Toradol) in 4-8ml 0.9% N/S x IV
 - ✎ OR **Inj. Tramadol 100mg/2ml** (Tramol) + **Inj. Dimenhydrinate 50mg/ml** (Gravinate) dilute in 100ml 0.9% NS. x IV
 - ✎ OR **Inj. Nalbuphine 10mg/ml** (Kinz) + **Inj. Dimenhydrinate 50mg/ml** (Gravinate) dilute in 100ml 0.9% NS. x IV
- **With Fever:** **Inj. Paracetamol 1g/100ml** (Provas) x IV x SOS/TDS (maximum 4 infusion/day)
- **If Spasmodic abdominal pain:**
 - ✎ **Inj. Drotaverine 40mg/2ml** (Nospa) x IV stat/TDS in 100ml 0.9% NS
 - ✎ OR **Inj. Phloroglucinol 40mg + Trimethylphloroglucinol 0.04mg/4ml** (Spasfon, Spasrid, Anafortan plus) dilute in 100ml 0.9% NS or Dextrose 5% x stat/BD/TDS
- **Inj. Omeprazole 40mg/vial** (Ruling, Omezol) diluted in 10ml 0.9% N/S x IV x OD
- **Consider IV empiric antibiotic therapy for intra-abdominal infection:**
 - ✎ **Inj. Metronidazole 500mg/100ml** (Flagyl) x IV x TDS
 - ✎ **PLUS one of the following:**
 - ✎ **Inj. Ceftriaxone 1g** (Oxidil, Titan, Rocephin) x IV x BD
 - ✎ OR **Inj. Cefuroxime 750mg** (Zinacef, Zecef) x IV x BD/TDS
 - ✎ OR **Inf. Ciprofloxacin 200mg/100 Or 400mg/100ml** (Novidate, Ciplet) x IV x BD
 - ✎ OR **Inj. Levofloxacin 750mg/150ml** (Leflox, Qumic) x IV x OD
 - ✎ OR **Inj. Moxifloxacin 400mg/250ml** (Moxiget, Mofest) x IV x OD
- **If severe infection or High Risk patient**
 - ✎ **Inj. Imipenem-Cilastatin 500mg-1g** (Cilapen, Tienam, Cilenem) x IV x TDS
 - ✎ OR **Inj. Meropenem 1g** (Meronem, Meroget, Penro) x IV x TDS
 - ✎ OR **Inj. Piperacillin-Tazobactam 4.5g** (Tanzo, Tazocin EF, Tazbac) x IV x TDS
- **With vomiting – consider ONE of the following anti-emetics:**
 - ✎ **Inj. Metoclopramide 10mg/2ml** (Metaclon) x IV x TDS
 - ✎ OR **Inj. Dimenhydrinate 50mg/ml** (Gravinate) x IV x TDS
 - ✎ OR **Inj. Ondansetron 8mg/4ml** (Onset, Onseron) x diluted in 50 to 100 ml of 0.9% NS OR D5%W, IV over 15 minutes.
- **Identify and treat the underlying cause.**



ACUTE APPENDICITIS



Acute Appendicitis

- Abdominal pain: Initial periumbilical pain 1st 24 hours with migration to the RLQ (because appendix is small gut organ & supplying is from small gut [Visceral nerve supply]).
- Right iliac Fossa pain (RIF) pain due to local irritation of parietal peritoneum by appendix.
- Nausea, vomiting & Fever.
- Sometime burning micturition due to irritation of ureter by appendix.

On examination:

- Always examine the sore throat for children
- ↑ Pulse rate (+/-)
- ↑ Temperature (+/-)
- Tender RIF/McBurney point tenderness
- Rebound tenderness (Local irritation)
- Psoas sign +ve: appendix touches the psoas muscle with full extension of the right hip, Associated with retrocecal appendix.
- Rovsing sign +ve: Pressing left iliac fossa causing pain in Right iliac fossa
- Obturator sign +ve: RLQ pain with right hip flexion followed by internal rotation.
- On Digital Rectal Examination: If pelvic appendix is present cause pain.

Labs findings:

- WBCs: ↑↑
- Urine R/E: Nitrates will be negative
- Urine pregnancy test in every child bearing age female to rule out ectopic pregnancy.

Imaging: U/S whole abdomen + Pelvic (to exclude other pathology in female)
 CXR, CT abdomen with contrast.

- Maintain ABCD&E
- Pass two large bore Intravenous cannulation
- Vitals monitoring: BP, PR, RR, Temperature, SpO₂
- obtained labs: CBC, BUN/Urea, creatinine, electrolyte, LFTs, PT APTT & INR, Viral marker (Anti HCV, HBsAg), RBS.
- No feeding by mouth (NPO-Bowel rest)
- Perform a focused history and physical examination.
- Pass Nasogastric (NG) tube and Foley's catheterization
- Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂
- Bowel care: if constipation give Syp. Lactulose/Skilex drop
- Start IV fluid therapy: RL x BD, 0.9% NS OR D5%W x IV x OD
- Correction of electrolytes imbalance
- Consider IV antibiotics therapy
 - Inj. Ceftriaxone 1g (Rocephin, Titan) x IV x BD PLUS
 - Inj. Metronidazole 500mg/100ml (Flagyl) x IV x TDS
- IV Pain management/analgesia:
 - Inj. Paracetamol 1g/100ml (Provas, Paracet) x IV x TDS/SOS
 - OR Inj. Ketorolac 30mg/ml (Toradol) in 4-8ml 0.9% N/S x IV
 - OR Inj. Tramadol 100mg/2ml (Tramol) + Inj. Dimenhydrinate 50mg/ml (Gravinate) dilute in 100ml 0.9% NS. x IV
 - OR Inj. Nalbuphine 10mg/ml (Kinz) + Inj. Dimenhydrinate 50mg/ml (Gravinate) dilute in 100ml 0.9% NS. x IV
- Inj. Omeprazole 40mg (Risek, Ruling) x IV diluted in 100ml 0.9% NS x OD
- With fever: Inj. Paracetamol 1g/100ml (Provas) x IV x SOS/TDS
- With vomiting – consider ONE of the following anti-emetics:
 - Inj. Metoclopramide 10mg/2ml (Metaclon) x IV x TDS
 - OR Inj. Dimenhydrinate 50mg/ml (Gravinate) x IV x TDS
 - OR Inj. Ondansetron 8mg/4ml (Onset, Onseron) x diluted in 50 to 100 ml of 0.9% NS OR D5%W, IV over 15 minutes.
- After complete workup, if indication of transfusion, arrange blood and shift the patient to Operation theater for Open or Laparoscopic Appendectomy

Alvarado score (MANTRELS) - 10 Points scoring system

	Characteristics	Score
Symptoms	» Migration of pain to RLQ	1
	» Anorexia	1
	» Nausea and/or vomiting	1
Physical examination	» Tenderness in RLQ	2
	» Rebound pain	1
	» Elevated temperature > 37.3°C (99.1°F)	1
Laboratory parameters	» Leukocytosis (> 10,000/mm ³)	2
	» Shift to the left ≥75% neutrophils	1

Likelihood of appendicitis → Low: ≤ 4, Moderate: 5-6, High: ≥ 7 (If score ≥ 7 = acute appendicitis)



ACUTE CHOLECYSTITIS

 Acute Cholecystitis

C/C:

Risk Factors: Fat, Female, Forty Flatulent, Fertile

Right hypochondriac (RHC) pain due to local irritation of peritoneum

- » Typically more severe and prolonged (> 6 hours) than in biliary colic
- » Postprandial
- » Radiation to the right shoulder (due to referred pain from dermatome/ phrenic nerve irritation)

Guarding

Fever, malaise, loss of appetite

Nausea and vomiting

On Physical Examination:

- » ↑ Pulse rate (+/-)
- » ↑ Temperature (+/-)
- » RHC tenderness to palpation
- » **Murphy sign +ve:** sudden pausing during inspiration upon deep palpation of the RHC due to pain, Murphy sign may be falsely negative in patients > 60 years.
- » **Boas sign:** hyperesthesia to light touch in RUQ or infrascapular area
- » Peritoneal signs may indicate perforation
- » Sometime a ball like structure is palpable by examiner hand due to swollen gall bladder.
- » Always look for jaundice

Investigation findings:

- » CBC: WBC ↑↑
- » LFTs: ↑/Normal
- » CRP: ↑↑
- » Serum amylase: exclude acute pancreatitis, (S/lipase most specific)
- » U/S whole abdomen (for gallstone)
- » X-ray erect abdomen (Shows Mercedes sign+ exclude enteric perforation "gas under diaphragm")
- » CT abdomen with IV contrast and HIDA scan



TREATMENT OF ACUTE CHOLECYSTITIS

1. Maintain ABCD&E
2. Pass two large bore Intravenous cannulation
3. Vitals monitoring: BP, PR, RR, Temperature, SpO₂
4. No feeding by mouth (NPO-Bowel rest) – 2-3 days
5. Perform a focused history and physical examination.
6. Obtained labs: CBC, Urea, Creatinine, electrolyte (U/C/E), LFTs, PT APTT & INR, serum amylase, Anti HCV, HBsAg, RBS & CRP
7. Pass Nasogastric (NG) tube → Aspiration through NG Tube: Aspiration of HCl decreases the stimulus to the secretion of bile. Spasm of gall bladder may come down. After 2-3 days, pain comes down, signs (tenderness) disappear and abdomen becomes soft.
NG tube is removed, clear oral fluid is given for 2-3 days followed by soft diet. After 6 weeks, the patient is advised to undergo elective cholecystectomy.
8. Foley's catheterization for urine output record
9. Bowel care: if constipation give Syp. Lactulose/Skilex drop
10. Start IV fluid therapy: R/L x BD, 0.9% N/S or Dextrose 5% x IV x OD
11. Correction of electrolytes imbalance
12. Start IV fluid: R/L x BD, 0.9% N/S OR Dextrose 5% x IV x OD
13. Consider IV empirical antibiotics therapy
 - ↳ Inj Metronidazole 500mg/100ml (Flagyl) x IV x TDS
 - ↳ PLUS
 - » Inj Cefuroxime 750mg (Zinacef) x IV x BD
 - » OR Inj. Ceftazidime 1g (Fortum, Fortazim) x IV x BD
 - » OR Inf. Ciprofloxacin 400mg/100ml (Novidate) x IV x BD
14. Inj. Omeprazole 40mg (Risek, Ruling) x IV x in 100ml 0.9% NS x OD
15. Pain management/analgesia:
 - ↳ Inj. Paracetamol 1g/100ml (Provas, Paracet) x IV x TDS/SOS
 - ↳ OR Inj. Ketorolac 30mg/ml (Toradol) in 4-8ml 0.9% N/S x IV
 - ↳ OR Inj. Tramadol 100mg/2ml (Tramol) + Inj. Dimenhydrinate 50mg/ml (Gravinate) dilute in 100ml 0.9% NS. x IV
 - ↳ OR Inj. Nalbuphine 10mg/ml (Kinz) + Inj. Dimenhydrinate 50mg/ml (Gravinate) dilute in 100ml 0.9% NS. x IV
16. With spasm: Inj Drotaverine 40mg to 80mg (Nospa, Relispa) OR Inj. Phloroglucinol+Trimethylphloroglucinol 40+0.04mg/4ml (Spasrid, Anafortan plus, Spasfon) x dilute in 100ml 0.9% Normal saline x IV x STAT

Note: Avoid Ceftriaxone because according to literature patient receiving ceftriaxone can develop acute cholecystitis: ceftriaxone-associated sludge can trigger existing gallstones to become symptomatic, ceftriaxone pseudolithiasis can transform into ceftriaxone gallstones, or the patient can become symptomatic from preexisting cholecystolithiasis unrelated to ceftriaxone therapy.

DIAGNOSTIC CRITERIA FOR ACUTE CHOLECYSTITIS

Local signs of inflammation	Murphy sign, RUQ pain, tenderness, or mass
Systemic signs of inflammation	Fever, ↑ CRP, Leukocytosis
Radiology findings	Any radiology finding characteristic of acute cholecystitis

Interpretation

Suspected diagnosis: ≥ 1 local sign of inflammation PLUS ≥ 1 systemic sign of inflammation

Definite diagnosis: ≥ 1 local sign of inflammation PLUS ≥ 1 sign of systemic inflammation PLUS any characteristic imaging finding

Definitive management

Grade-I Acute Cholecystitis

- Low surgical risk: early laparoscopic cholecystectomy
- High surgical risk
 - » Start Empiric antibiotic therapy and general supportive care.
 - » Once the patient's condition has improved, perform early laparoscopic cholecystectomy (if feasible) or delayed laparoscopic cholecystectomy
 - » Discontinue antibiotics 24 hours after surgery (if early laparoscopic cholecystectomy) or until symptomatic improvement (if delayed laparoscopic cholecystectomy).

Grade-II Acute Cholecystitis

- Start Empiric antibiotic therapy (1st choice Piperacillin-tazobactam, Moxifloxacin, Meropenem, 2nd is metronidazole plus combination with cephalosporins) and general supportive care.
- Improvement with antibiotic therapy:
 - » Low surgical risk: early laparoscopic cholecystectomy
 - Discontinue antibiotics 24 hours after surgery.
 - » High surgical risk: delayed laparoscopic cholecystectomy
 - Continue antibiotic therapy until symptomatic improvement.
- No improvement with antibiotic therapy: urgent elective interval cholecystectomy
 - » Continue antibiotics for a total of 7 days.

Grade-III Acute Cholecystitis

- Start Empiric antibiotic therapy and general supportive care.
- Provide hemodynamic and respiratory support.
- Low surgical risk: early laparoscopic cholecystectomy if there is an adequate response to initial supportive care – Continue antibiotics for 4–7 days after surgery.
- High surgical risk: Elective interval cholecystectomy OR observation
 - » Continue antibiotics for a total of 7 days.

Laparoscopic Cholecystectomy

- Indication: gold standard of treatment for acute calculous cholecystitis
- Timing: depends on surgical and anesthesia risks, disease severity, and symptom duration
 - » Early laparoscopic cholecystectomy: performed within 10 days of symptom onset; preferably within the initial 24–72 hours
 - » Indication: symptom duration of ≤ 10 days in patients with low surgical and anesthesia risk(s)
- Contraindications
 - High surgical or anesthesia risks
 - Symptom duration > 10 days
- » Interval laparoscopic cholecystectomy (delayed laparoscopic cholecystectomy):
 - Performed 45 days after resolution of symptoms
 - Indications: High surgical or anesthesia risk and Symptoms duration > 10 days

Emergency Cholecystostomy

- About 10% of cases of acute cholecystitis require emergency cholecystostomy.
- In these patients, high grade fever, sepsis, shock, high leukocyte count are the deciding factors.
- Acalculous cholecystitis and perforated gall bladder with peritonitis are definitely strong indications for emergency cholecystostomy.



CHOLELITHIASIS (GALLSTONES)

- Definition: Cholelithiasis refers to the presence of abnormal concretions (gallstones) in the gallbladder. Gallstones most commonly consist of cholesterol but may be pigmented or mixed.
- Sex: Female > male (2-3:1), Peak incidence: > 40 years
- Risk factors: Rule of the 6 Fs: Fat, Female, Fertile, Forty, Fair-skinned, Family history.

△ Cholelithiasis

C/C:

- Most gallstones are asymptomatic.
- Biliary colic:** constant, dull RUQ pain lasting < 6 hours
 - Especially postprandial: vagal stimulation (e.g., cholecystokinin release following a fatty meal) → gallbladder contraction → attempts to force the stone into the cystic duct
 - May radiate to the epigastrium, right shoulder, and back (referred pain)
- Nausea and vomiting
- Early satiety
- Bloating
- Dyspepsia

Diagnostic workup:

- Laboratory test** are typically normal in uncomplicated cholelithiasis but should be ordered to rule out other acute biliary conditions and/or other causes of acute abdominal pain
- Radiological test:**
 - Ultrasound Abdomen (Investigation of choice)
 - MRI abdomen without and with IV contrast with MRCP (Second line investigation)
 - CT abdomen with IV contrast (If MRI is not available)
 - MRI without contrast is preferred in pregnant patients.

X-ray and CT scan are rarely diagnostic in cholelithiasis because only 15-20% of stones are radiopaque. Pure cholesterol stones are radiolucent

Rx

- Maintain ABCD&E
- Pass two large bore Intravenous cannulation
- Vitals monitoring: BP, PR, RR, Temperature, SpO₂
- No feeding by mouth (NPO-Bowel rest)
- Perform a focused history and physical examination.
- obtained labs: CBC, Urea & Creatinine, electrolytes, LFTs, PT APTT & INR, serum amylase, Anti HCV, HBsAg, RBS & CRP
- Pass Nasogastric tube and Foley's catheterization
- Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂
- Bowel care: if constipation advice Syp. Lactulose/Skilex drop
- Start IV fluid therapy: R/L x BD, 0.9% N/S Or Dextrose 5% x IV x OD
- Correction of electrolytes imbalance
- Consider IV Empirical antibiotics therapy
 - Inj. Metronidazole 500mg/100ml (Flagyl) x IV x TDS
 - PLUS
 - Inj. Cefuroxime 750mg (Zinacef) x IV x BD
 - OR Inf. Ciprofloxacin 400mg/100ml (Novidate) X IV X BD
 - OR Inj. Ceftazidime 1g (Fortum, Fortazim) X IV X BD
- Inj. Omeprazole 40mg/vial (Risek, Ruling) x IV x in 100ml 0.9% NS x OD
- Pain management/analgesia:
 - Inj. Paracetamol 1g/100ml (Provas, Paracet) x IV x TDS/SOS
 - OR Inj. Ketorolac 30mg/ml (Toradol) in 4-8ml 0.9% N/S x IV
 - OR Inj. Tramadol 100mg/2ml (Tramol) + Inj. Dimenhydrinate 50mg/ml (Gravinate) dilute in 100ml 0.9% NS. x IV
 - OR Inj. Nalbuphine 10mg/ml (Kinz) + Inj. Dimenhydrinate 50mg/ml (Gravinate) dilute in 100ml 0.9% NS. x IV
- With spasm: Inj Drotaverine 40mg to 80mg (Nospa, Relispa) OR Inj. Phloroglucinol+Trimethylphloroglucinol 40+0.04mg/4ml (Spasrid, Anafortan plus, Spasfon) x dilute in 100ml 0.9% Normal saline x IV x STAT

Procedure of choice: Elective Laparoscopic cholecystectomy



CHOLEDOCOLITHIASIS

Cholelithiasis

- Right Upper Quadrant pain
 - More severe and prolonged (may last > 6 hours) than in cholelithiasis
 - Postprandial
 - May radiate to the epigastrium, right shoulder, and back (referred pain)
- Nausea, vomiting, anorexia
- Signs of extrahepatic cholestasis (e.g., jaundice, pale stool, dark urine, pruritus) may be present
- Features of complications: See "Clinical features" in acute pancreatitis, acute cholecystitis, and acute cholangitis

Send labs: CBC, Urea, creatinine, electrolyte (U/C/E), LFTs e gamma GT and Alkaline phosphatase (Characteristic findings: evidence of cholestasis -↑ ALP, ↑ GGT, ↑ total and ↑ direct bilirubin), Amylase, Lipase, PT & INR, Viral marker (Anti HCV, HBsAg)

Imaging:

- Ultrasound:** First test, can document GB stones and estimate the CBD diameter
- A dilated bile duct (>8 mm in diameter) in a patient with gallstones, jaundice and biliary pain is highly suggestive of choledocholithiasis.
- CT scan abdomen with contrast**
- MRCP:** Provides excellent anatomic detail, with sensitivity and specificity of 95% and 98%, respectively, for CBD stones.
- ERCP:** Diagnostic and therapeutic test of choice for patients with suspected CBD stones

Surgical Treatment option:

- ERCP-guided stone extraction
- Laparoscopic Bile Duct Exploration (LBCDE)
- Mechanical and laser lithotripsy
- Elective interval cholecystectomy
 - Goal:** recurrence prevention
 - Procedure:** Laparoscopic Cholecystectomy



- Treatment is recommended in all patients with choledocholithiasis, even if asymptomatic.
- The mainstay of treatment is the removal of the obstruction.

- Maintain ABCD&E
- Pass two large bore Intravenous cannulation
- Vitals monitoring: BP, PR, RR, Temperature, SpO2
- Send initial labs and perform imaging
- No feeding by mouth (NPO-Bowel rest)
- Perform a focused history and physical examination.
- Pass Nasogastric (NG) tube and Foley's catheterization
- Vitals monitoring: Check BP, PR, RR, Temperature, SpO2
- Bowel care: if constipation give Syp. Lactulose/Skilex drop
- Start IV fluid therapy: Ringer Lactate, 0.9% N/S OR Dextrose 5% x IV
- Correction of electrolytes imbalance
- Empiric IV antibiotic therapy
 - Inj. Metronidazole 500mg/100ml (Flagyl) x IV x TDS PLUS
 - Inj. Ceftriaxone 1g (Rocephin, Titan) x IV x BD
 - OR Inf. Ciprofloxacin 400mg/100ml (Novidate) x IV x BD
 - OR Inj. Ceftazidime 1g (Fortum, Fortazim) x IV x BD
 - OR Inj. Cefepime 1g (Uceph, Cefstar) x IV x BD
 - If severe infection/Grade-II, Grade-III & High risk patients
 - OR Inj. Imipenem-cilastatin 500mg-1g (Tienam) x IV x TDS
 - OR Inj. Meropenem 1g (Meronem, Meroget) x IV x TDS
 - OR Inj. Piperacillin-tazobactam 4.5g (Tanzo) x IV x TDS
- IV pain management/analgesia:
 - Inj. Ketorolac 30mg/ml (Toradol) in 4-8ml 0.9% N/S x IV
 - OR Inj. Buprenorphine 0.3mg/ml (Buepron, Norpin) + Inj. Dimenhydrinate 50mg/ml (Gravinate) dilute in 100ml 0.9% NS. x IV
 - OR Inj. Nalbuphine 10mg/ml (Kinz) + Inj. Dimenhydrinate 50mg/ml (Gravinate) dilute in 100ml 0.9% NS. x IV
- Inj. Omeprazole 40mg (Risek, Ruling) x IV x in 100ml 0.9% NS x OD
- Fever/analgesia: Inj. Paracetamol 1g/100ml (Provas) x IV x SOS/TDS
- With vomiting – consider ONE of the following anti-emetics:
 - Inj. Metoclopramide 10mg/2ml (Metaclon) x IV x TDS
 - OR Inj. Dimenhydrinate 50mg/ml (Gravinate) x IV x TDS
 - OR Inj. Ondansetron 8mg/4ml (Onset, Onseron) x diluted in 50 to 100 ml of 0.9% NS OR D5%W, IV over 15 minutes.



ACUTE CHOLANGITIS

△ Acute Cholangitis

C/C:

- » **Charcot cholangitis triad** (25–70% of patients present with all three features)
 1. Most commonly RUQ Abdominal pain
 2. High fever
 3. Jaundice (least common feature)
- » **Reynolds pentad:** Charcot cholangitis triad **PLUS** hypotension and mental status changes
- » Features of sepsis, septic shock, and multiorgan dysfunction may be present, depending on the severity of disease at presentation.
- » Elderly patients may present with nonspecific symptoms such as confusion; pain and jaundice may be absent.

Diagnostic workup

Tests to support the clinical diagnosis

- » **CBC:** leukocytosis with left shift
- » **CRP:** elevated
- » **LFTs:** signs of cholestasis (↑ bilirubin, ↑ GGT, ↑ ALP, ↑ ALT)
- » **Blood cultures (2 sets):** Obtain before administering antibiotics (especially in febrile patients).
- » **Bile cultures:** obtain during biliary drainage procedure

Tests to assess severity of disease

- » **Blood gas analysis:** PaO₂/FIO₂ ratio < 300 in severely ill patients
- » **Urea, creatinine & electrolytes (UCE):** AKI, electrolyte derangements in patients with severe disease
- » **PT/INR:** coagulopathy in patients with severe disease

Tests to evaluate differential diagnoses

- » Consider serum lipase levels to assess for concurrent biliary pancreatitis in patients with suspected common bile duct obstruction.

Radiological Investigation (Explained below)

Diagnosis: Acute cholangitis is diagnosed based on systemic signs of inflammation (fever, leukocytosis, ↑ CRP) in combination with signs of cholestasis (jaundice, ↑ GGT, ↑ ALP) and/or characteristic imaging findings (e.g., dilated CBD, periductal inflammation).

Urgent gastroenterology, interventional radiology, and/or surgery consult for biliary drainage and decompression

Rx

TREATMENT OF ACUTE CHOLANGITIS

1. **Maintain ABCD&E**
2. **Pass two large bore Intravenous cannulation**
3. **Send 2 sets of Blood cultures**
4. **Send initial labs:** CBC, Urea, Creatinine, & electrolyte (U/C/E), LFTs, PT, APTT & INR, Viral marker (Anti HCV, HBsAg), RBS and other important labs
5. **Vitals monitoring:** BP, PR, RR, Temperature, SpO₂
6. **No feeding by mouth (NPO-Bowel rest)**
7. **Perform a focused history and physical examination.**
8. **Pass Nasogastric (NG) tube and Foley's catheterization**
9. **Vitals monitoring:** Check BP, PR, RR, Temperature, SpO₂
10. **Bowel care:** if constipation give Syp. Lactulose/Skilex drop
11. **Start IV fluid therapy:** Ringer Lactate x BD, 0.9% N/S OR Dextrose 5% x IV x OD
12. **Correction of electrolytes imbalance**
13. **Empiric IV antibiotic therapy for acute biliary infection**
 - ✦ **Inj. Metronidazole 500mg/100ml (Flagyl) x IV x TDS PLUS**
 - ✦ **Inj. Ceftriaxone 1g (Rocephin, Titan) x IV x BD**
 - ✦ **OR Inf. Ciprofloxacin 400mg/100ml (Novidate) X IV X BD**
 - OR Inj. Ceftazidime 1g (Fortum, Fortazim) X IV X BD**
 - OR Inj. Cefepime 1g (Uceph, Cefstar) X IV X BD**
- If Severe Infection/Grade-II, Grade-III & High Risk Patients**
 - ✦ **OR Inj. Imipenem-Cilastatin 500mg-1g (Tienam) X IV X TDS**
 - OR Inj. Meropenem 1g (Meronem, Meroget) X IV X TDS**
 - OR Inj. Piperacillin-Tazobactam 4.5g (Tanzo) X IV X TDS**
14. **IV Analgesic for Pain Management:**
 - ✦ **Inj. Ketorolac 30mg/ml (Toradol) in 4ml 0.9% N/S x IV**
 - ✦ **If not respond/severe pain then give Inj. Tramadol 100mg/2ml (Tramol), OR Inj Nalbuphine 10mg/ml (Kinz) PLUS with Inj. dimenhydrinate 50mg/ml (Gravinate) dilute in 8ml 0.9% N/S or D/W x give slow IV. (Or dilute in 100ml 0.9% NS)**
15. **Inj. Omeprazole 40mg (Risek, Ruling) x IV x in 100ml 0.9% NS x OD**
16. **With Fever:** Inj. Paracetamol 1g/100ml (Provas) x IV x SOS/TDS
17. **With vomiting – consider ONE of the following anti-emetics:**
 - ✦ **Inj. Metoclopramide 10mg/2ml (Metaclo) x IV x TDS**
 - ✦ **OR Inj. Dimenhydrinate 50mg/ml (Gravinate) x IV x TDS**
 - ✦ **OR Inj. Ondansetron 8mg/4ml (Onset, Onseron) x diluted in 50 to 100 ml of 0.9% NS OR D5%W, IV over 15 minutes.**

RADIOLOGICAL INVESTIGATION FOR ACUTE CHOLANGITIS

- Acute cholangitis cannot be diagnosed with imaging alone.
- The goal of imaging is to evaluate for biliary obstruction that may have precipitated cholangitis.
- RUQ ultrasound is not sufficiently sensitive to definitively rule out biliary obstruction.
- Obtain cross-sectional imaging (CT abdomen or MRCP) in patients with a high pretest probability of acute cholangitis and a negative RUQ ultrasound

Right Upper Quadrant (RUQ) ultrasound

Indication: preferred first-line imaging modality in patients presenting with suspected cholangitis

Supportive findings

- Dilated common bile duct
- Dilated intrahepatic bile ducts: indicates obstructive cholestasis
- Thickened bile duct walls
- Evidence of underlying etiology, such as:
 - Cholelithiasis:** occluding CBD stone with/without cholelithiasis may be visualized
 - Biliary stricture:** focal narrowing of the bile duct(s), with dilation of the proximal biliary tree
 - Biliary tumor:** intraluminal mass within the bile duct

CT scan abdomen with IV contrast

Indications

- Confirmatory imaging modality if ultrasound is inconclusive
- To rule out differential diagnoses if the clinical diagnosis is unclear

Supportive findings

- Concentric thickening and heterogeneous enhancement of the walls of the biliary tree
- Bile duct dilation
- Periductal edema
- Evidence of underlying cause:** choledocholithiasis, biliary tumor, biliary-enteric fistula, hydatid cyst, etc.
- Evidence of complications:** pericholecystic or liver abscess, portal vein thrombosis

MRI abdomen without and with IV contrast with MRCP

- Indication:** an alternative confirmatory imaging modality if ultrasound is inconclusive
- Supportive findings:** similar to CT findings

DIAGNOSTIC CRITERIA FOR ACUTE CHOLANGITIS

Charcot triad is not included in the diagnostic criteria because, although specific, it is not a sensitive criterion and may even be absent in patients with acute cholangitis.

Systemic signs of inflammation	- Fever and/or chills with rigors Laboratory findings: ↑ WBC, CRP
Signs of cholestasis	- Jaundice LFTs: signs of cholestasis (↑ bilirubin, ↑ GGT, ↑ ALP, ↑ ALT)
Imaging findings	- Biliary dilatation - Evidence of underlying etiology (maybe choledocholithiasis, biliary stricture, biliary stent, etc.)

Interpretation

- Suspected diagnosis:** ≥ 1 sign of inflammation **PLUS** either ≥ 1 sign of cholestasis **OR** ≥ 1 characteristic imaging findings
- Definite diagnosis:** ≥ 1 sign of inflammation **PLUS** ≥ 1 sign of cholestasis **PLUS** ≥ 1 characteristic imaging findings

SEVERITY GRADING FOR ACUTE CHOLANGITIS

- Once the diagnosis is confirmed, disease severity should be assessed to determine the best approach to treatment

Grades of severity	Grading criteria
Grade-I (Mild acute cholangitis)	- Acute cholangitis with no evidence of organ dysfunction - Does not meet any criteria of grade II or III acute cholangitis
Grade-II (Moderate acute cholangitis)	Acute cholangitis PLUS any two of the following: - WBC count > 12,000/mm³ or < 4,000/mm³ - Temperature ≥ 39°C - Age ≥ 75 years - Total serum bilirubin ≥ 5 mg/dL - Serum albumin less than 70% of lower limit of normal
Grade-III (Severe acute cholangitis)	Dysfunction of at least one organ system Cardiovascular: hypotension requiring treatment with dopamine ≥ 5 mcg/kg/minute or any dose of norepinephrine Neurologic: impaired consciousness Respiratory: PaO₂/FIO₂ ratio < 300 Renal: oliguria, serum creatinine > 2 mg/dL Hepatic: INR > 1.5 Hematologic: platelet count < 100,000/mm³



ANAL FISSURE

△ Anal Fissure

C/C:

- » Severe pain on defaecation.
- » Constipation
- » Perianal pain & itching
- » Perianal irritation
- » Bleeding is usually small (Bright red blood) and occurs as a streak by the side of stools.

- » On examination, a longitudinal ulcer is seen in the midline posteriorly that maybe covered by a skin tag. There is local inflammation and induration



Medicated Disposable Sitz Bath



Rx CONSERVATIVE TREATMENT OF ANAL FISSURE

General measures for anal fissure

- » Adequate fluid intake (6-8 glasses of liquids)
- » Avoid constipation
- » Advise fiber rich diet to prevent constipation i.e vegetables, fruits, brown rice.
- » Bulk forming agents (psyllium husk, bran)
- » Sitz bath - sitting in a tub containing lukewarm water provide relief from spasm and pain or containing warm antiseptic lotion
- » Once recovers, regular anal dilatation

Pharmacotherapy

1. Tab Metronidazole 400mg (Flagyl/Metrozine)
1 + 1 + 1 (TDS)

Consider antibiotics if soft tissue infection:

2. Cap Cephalexin 250mg, 500mg (Ceporex, Keflex) x TDS/BD
OR Cap Cefixime 400mg (Cefiget) x OD

3. Cap Esomeprazole 40mg (Eso/Nexum)
0 + 0 + 1

کھانے سے 30 منٹ پہلے

4. Glyceryl tri nitrate 2% ointment (GTN)
1 + 0 + 1

» Topical nitroglycerine 0.2% is also used to relax the sphincter. It causes severe headache.

5. Lidocaine 2% jelly (Xyloaid/Lignocaine)
1 + 0 + 1

6. Syt Lactulose 30ml (Duphalac/Lilac)
0 + 0 + 1

SITZ BATH

Sitz bath is used after perineal surgeries like for piles, fissure, and fistula.

Patient sits in warm water bath with perineum dipped in the water. Often small quantity of antiseptics or KMNO₄ is added.

Duration of setting: 15-20 minutes

Warm water is used, Warm water is a vasodilator, which means that it causes blood vessels to open and muscles to relax. By loosening the tightened and swollen piles, it eases the pain and the swollen portion may even shrink.

HEMORRHOIDS (Urdu = بواسیر)



CONSERVATIVE TREATMENT OF HEMORRHOIDS

△ Hemorrhoids/Piles

- » Many small sized haemorrhoids are asymptomatic
- » Painless bleeding (bright red) that can be mild or severe.
- » Mucous discharge, prolapse of piles and occasionally pain due to proctitis
- » Chronic cases develop anaemia due to continuous blood loss.

Internal Hemorrhoids

- » Located proximal to the dentate line
- » Painless, can be ligated
- » Banding is preferred

External Hemorrhoids

- » Located distal to dentate line
- » Also known as 5-days painful self-curing lesion
- » Painful, not ligated
- » Excision is done
- » Repeated thrombosis leads to semi-ripe black currant appearance

Consider antibiotics if infection

- » Tab Ciprofloxacin 500mg x BD
- » Cap Cefixime 400mg x OD

Medical therapy: Bleeding from 1st and 2nd degree hemorrhoids often improve with the addition of dietary fibre, stool softeners and other diet regulation

1. **Tab. Micronized purified flavonoid fraction (MPFF) 500mg (Daflon)**
2 Tablets x BD/TDS
2. **Topical Lidocaine 2% jelly (Xyloaid, Lignocaine)**
1-0-1 (apply twice daily with the help of using finger or applicator)
3. **Topical Posterison forte ointment OR Hadensa forte Ointment**
1-0-1 (apply twice daily with the help of using finger or applicator)
4. **If Constipation is a problem:** Give stool softners and increase roughage in diet
Syp Lactulose 30ml (Duphalac, Lilac)
0-0-30ml x HS
5. **Cap. Omeprazole 40mg (Risek, Ruling)**
0-0-1

کھاتے سے 30 منٹ پہلے

If severe rectal pain → Systemic painkiller

6. **Tab. Diclofenac sodium 50mg, 100mg (Voren, Voltral) x BD**
OR **Tab. Tramadol + Paracetamol (Distalgescic, Pentra Plus) x BD**
7. **Chronic cases develop anaemia** due to continuous blood loss so send CBC, PT & INR and Correct anaemia with oral ferrous sulphate, Inj. Iron Sucrose or blood transfusion if indicated

Surgery: If not Responded to the treatment OR Late third and fourth degree Haemorrhoids go with surgical correction.

- » **NPO patient**
- » **IV hydration, pain management and IV antibiotics to cover infection**
- » **Send Labs: CBC, PT INR, Urea, creatinine and electrolytes**
- » **After complete workup send to operation theater.**

CLASSIFICATION OF INTERNAL HEMORRHOIDS ON THE BASIS OF CLINICAL FEATURES

1. First Degree	Painless bleeding only, No prolapse
2. Second Degree	Bleeding occurs, Prolapse through the anus, on straining but reduce spontaneously
3. Third Degree	Piles Prolapse during defaecation through the anal canal and require manual reduction
4. Fourth Degree	Piles are large, Permanently prolapsed and cannot be manually reduced.

TREATMENT OPTION OF HEMORRHOIDS

Rubber band ligation	» Done for 1st, 2nd and selected 3rd degree hemorrhoids
Infrared photocoagulation	» Done for 1st and 2nd degree hemorrhoids
Sclerotherapy	» Done for 1st, 2nd and selected 3rd degree hemorrhoids » Most commonly used sclerosant is 5% phenol in almond or arachis oil
Operative haemorrhoidectomy	» 3rd and 4th degree hemorrhoid
» Milligan-Morgan open haemorrhoidectomy	» 2nd degree not cured by non-operative methods
» Ferguson closed haemorrhoidectomy	» Mixed (combine internal/external hemorrhoids)
» Whitefield submucosal haemorrhoidectomy	» Fibrosed hemorrhoids
» Longo's stapler haemorrhoidectomy	



ANO-RECTAL ABSCESS

- Acute sepsis in the region of the anus is common.
- More common in men, Most Common organism responsible: *E. coli* > *Bacteroides*
- Subdivided into:** Perianal (Most Common), Ischiorectal (2nd Most Common), submucous & pelvirectal
- Underlying conditions:** Fistula-in-ano (Most Common), Crohn's disease, diabetes, immunosuppression

△ Ano-rectal Abscess

C/C:

- Usually produces a painful, throbbing swelling in the anal region with swinging pyrexia
- Patients with infection in the larger fatty-filled ischiorectal space, in which tissue tension is much lower, usually present later, with less well localized symptoms but more constitutional upset & fever.

Rx

- Always look for a potential underlying problem
- Bowel care:** if constipation give syp. Lactulose/Skilex drop
- Surgical Drainage of pus**
- IV antibiotics:** Inj Ceftriaxone 1-2g (Titan) x IV STAT
- If fever:** Inj Paracetamol 1g/100ml (Provas) x IV STAT
- Pain:** Inj. Ketorolac 30mg (Toradol) in 4-8ml 0.9% N/S x IV
- Discharge on**
 - Tab. Co-amoxiclav 1g (Augmentin) x BD
OR Cap. Cefixime 400mg (Cefiget, Cefspan) x OD
 - Tab. Paracetamol 500mg (Panadol) x TDS/QID
OR Tab. Mefenamic acid 500mg (Ponstan forte) x TDS

PILONIDAL SINUS

- Acquired disease, seen in hairy males, seen in age group of 20-29 years, Common among military personnel, also known as 'jeep disease, prolonged sitting on hard surfaces.
- Location:** Found in the natal cleft overlying the coccyx

△ Pilonidal Sinus

C/C:

- Characteristically seen in dark-haired individuals rather than those with softer blond hair
- Patients complain of intermittent pain, swelling & discharge at the base of the spine
- History of repeated abscesses that have burst spontaneously or which have been incised, usually away from the midline

Rx

Conservative treatment for minor symptoms

- Simple cleaning out of tracks and removal of all hair, with regular shaving of the area
- Strict hygiene may be recommended.
 - Tab. Co-amoxiclav 1g (Augmentin) x BD
OR Cap. Cefixime 400mg (Cefiget, Cefspan) x OD
 - Tab. Paracetamol 500mg (Panadol) x TDS/QID
OR Tab. Mefenamic acid 500mg (Ponstan forte) x TDS
- Treatment of an acute exacerbation (abscess):**
Abscess drainage with thorough curettage of granulation tissue and hair

SURGICAL TREATMENT OF CHRONIC PILONIDAL DISEASE

- Laying open of all tracks with or without marsupialisation
- Excision of all tracks with or without primary closure
- Excision of all tracks & closure by Limberg's flap, Karydakis flap or rhomboid flap
- Bascom's procedure:** Incision lateral to the midline to gain access to the sinus cavity, which is rid of hair & granulation tissue and excision & closure of the midline pits. The lateral wound is left open



ACUTE PANCREATITIS

CAUSES OF PANCREATITIS (MNEMONIC AS "I GET SMASHED")

- » Idiopathic (25%), Infections (Bacterial, Parasitic, Viral)
- » Gallstones (~ 40% of cases)
- » Ethanol Alcohol (20% of cases)
- » Trauma: iatrogenic or blunt abd. trauma to pancreas
- » Structural anomalies: Pancreas divisum, annular pancreas
- » Mumps, Malignancy
- » Autoimmune
- » Scorpion sting, Spider sting bite
- » Hypertriglyceridemia, Hypercalcaemia, Hereditary (e.g., mutation of PRSS1 gene, cystic fibrosis)
- » ERCP (Post ERCP)

- » Drugs:
 - » Steroids
 - » Statins
 - » Azathioprine
 - » Antibiotics: Sulfonamides, metronidazole and tetracycline
 - » Loop and thiazide diuretics
 - » Estrogen
 - » HIV therapy: Didanosine, Pentamidine
 - » NRTIs: Abacavir
 - » Anticonvulsants: valproate sodium

SEVERITY GRADING AND PROGNOSTIC SCORES OF PANCREATITIS

There are several scores used to assess the severity and prognosis of acute pancreatitis. The most commonly used and validated scores are described here.

REVISED ATLANTA GRADES OF SEVERITY

The revised Atlanta grades of severity classify pancreatitis as mild, moderate, or severe, depending on the presence of organ failure. Organ failure can be determined using the modified Marshall scoring system for organ dysfunction.

- » Mild acute pancreatitis: no organ failure and no local or systemic complications
- » Moderate acute pancreatitis: transient organ failure (< 48 hours) and/or local or systemic complications
- » Severe acute pancreatitis: persistent organ failure (> 48 hours)

CT severity index

The CT severity index for acute pancreatitis (CTSI) and modified CT severity index (MCTSI) can be used to estimate the severity, mortality, and morbidity of acute pancreatitis based on the extent of pancreatic inflammation and necrosis on a CT abdomen performed ideally > 5–7 days (or at least 72 hours) after symptom onset.

CT severity index for acute pancreatitis (CTSI) and modified CT severity index (MCTSI)

Features		CTSI	MCTSI
Degree of inflammation	Normal pancreas	0	0
	Localized or diffuse enlargement	1	2
	Peripancreatic inflammation	2	4
	Single acute fluid collection	3	
	Multiple or extensive acute fluid collections	4	
Degree of parenchymal necrosis	None	0	0
	< 30%	2	2
	≥ 30% – 50%	4	4
	> 50%	6	2
Presence of extra-pancreatic complications		N/A	

Interpretation:

- » CTSI: Mild: 0–3 points, Moderate: 4–6 points, Severe: 7–10 points.
- » MCTSI: Mild: 0–2 points, Moderate: 4–6 points, Severe: 8–10 points



Ranson criteria for acute pancreatitis - Predict mortality

The Ranson criteria is one of the oldest predictive models used to estimate severity and prognosis of biliary and non-biliary pancreatitis, but full assessment is only possible after 48 hours, and sensitivity for predicting severity and outcome can be as low as 70%.

Parameter	Non-biliary pancreatitis	Biliary pancreatitis
	On admission	
Age	> 55 years	> 70 years
WBC	> 16,000/mm ³	> 18,000/mm ³
Blood glucose	> 200 mg/dL	> 220 mg/dL
Serum LDH	> 350 U/L	> 400 U/L
Serum AST	> 250 U/L	> 250 U/L
Parameter	After initial 48 hours	
Hematocrit (Hct)	> 10%	> 10%
BUN increase	> 5 mg/dL	> 2 mg/dL
Serum calcium	< 8 mg/dL	< 8 mg/dL
Arterial pO ₂	< 60 mm Hg	N/A
Fluid sequestration	> 6 L	> 4 L
Serum base deficit	> 4 mmol/L	> 5 mmol/L

Interpretation

- Each criterion is worth one point.
- Composite score of ≥ 3 : high risk for severe acute pancreatitis

Acute physiology and chronic health evaluation II (APACHE II score)

- Mainly used in the ICU setting to determine the severity of acute pancreatitis
- Scores ≥ 8 indicate severe pancreatitis with a guarded prognosis.
- See online calculator of APACHE SCORE
 - <https://www.mdcalc.com/apache-ii-score>
 - <https://clincalc.com/icuMortality/APACHEII.aspx>

Bedside index of severity of acute pancreatitis (BISAP)

- Used to estimate in-hospital mortality due to pancreatitis
- Each criterion is worth one point.
 - BUN > 8.9 mmol/L
 - Altered mental status
 - Presence of SIRS
 - Age > 60 years
 - Pleural effusion on chest x-ray
- BISAP ≥ 2 indicates severe pancreatitis.

CLINICAL FEATURES

- Constant, severe epigastric pain**
 - Classically radiating towards the back
 - Worse after meals and when supine
 - Improves on leaning forwards
 - Nausea, vomiting
- General physical examination**
 - Signs of shock: tachycardia, hypotension, oliguria/anuria
 - Possibly jaundice in patients with biliary pancreatitis
- Abdominal examination**
 - Abdominal tenderness, distention, guarding ileus with reduced bowel sounds and tympany on percussion
 - Ascites
 - Skin changes (rare)
 - Cullen's sign: periumbilical ecchymosis and discoloration (bluish-red)
 - Grey Turner's sign: flank ecchymosis with discoloration



Diagnostic workup

- » CBC: Hct ↑, WBC ↑
- » ↑ Markers of volume status and tissue perfusion
 - Blood urea nitrogen (BUN)
 - Creatinine
 - Lactate
- » ↑ Blood glucose level
- » Abnormal serum calcium (Ca^{++})
 - ↓ Ca^{++} : indicates saponification
 - ↑ Ca^{++} : can cause acute pancreatitis
- » Inflammatory markers
 - ↑ CRP: Levels > 150 mg/L 3 days after onset can indicate severe or necrotizing pancreatitis
 - ↑ Procalcitonin: sensitive for infected necrosis
 - ↑ Interleukin-6 (IL-6): can be seen in infected necrosis and used as a predictor for remote organ failure
- » Liver enzyme (LFTs) findings suggestive of biliary pancreatitis
 - ↑ Aminotransferases: ALT > 150 U/L, AST > 3x ULN
 - ↑ Cholestasis markers: bilirubin (total and direct), alkaline phosphatase (ALP), GGT
- » ↑ LDH: a marker of severity; high levels are suggestive of necrotizing pancreatitis
- » ↑ Serum triglyceride (fasting): can be considered the cause of acute pancreatitis at levels > 1,000 mg/dL
- » Serum Amylase (most sensitive), and serum Lipase (most specific test)

Imaging

- » Whole Abdominal USG
- » MRI abdomen > CT scan abdomen with contrast
- » Magnetic resonance cholangiopancreatography (MRCP)
 - Indications: prior to therapeutic ERCP in suspected biliary pancreatitis.
- » Endoscopic retrograde cholangiopancreatography (ERCP)
 - Indications
 - Suspected choledocholithiasis (if MRCP or MRI are not feasible) and To evaluate for sphincter of Oddi dysfunction in patients with recurrent pancreatitis and normal or inconclusive EUS and MRCP
- » Chest x-ray, ECG & Echocardiography.

Rx

1. Maintain ABCD&E
2. Start oxygen therapy if hypoxic
3. Establish IV access with two large-bore cannulas.
 - » Send laboratory investigations.
 - » Perform ABG.
4. Maintain NPO status until potential causes of acute abdomen that require emergency surgery have been ruled out.
5. Pass Nasogastric tube and Foley's catheterization
 - Nasogastric tube insertion; not routinely recommended; indicated in patients with vomiting and/or significant abdominal distention
6. Vitals monitoring: BP, PR, RR, Temperature, SpO₂
7. Bowel care: if constipation give Lactulose/Skilex drop
8. Goal-directed IV fluid therapy
 - Fluids and infusion rat
 - » Crystalloids such as normal saline (NS) or Ringer lactate (LR) are preferred.
 - Hemodynamically stable patients
 - 5–10 mL/kg/hour or 250–500 mL/hour
 - Exercise caution in patients with renal or cardiovascular disease.
 - Hemodynamically unstable patients
 - Administer rapid fluid bolus: NS or LR 500–1000 mL IV bolus over 10–30 minutes.
 - Repeat as needed based on response.
 - Fluid therapy goals in acute pancreatitis
 - » Heart rate: < 120 bpm, MAP 65–85 mm Hg
 - » Urine output: > 0.5–1 mL/kg/hour
 - » Central venous pressure: 8–12 mm Hg, central venous oxygen saturation ≥ 70%
 - » Hematocrit (Hct): 35–44%
9. Replete electrolytes as needed.
10. Gastroprotective: Inj Omeprazole 40mg (Risek, Ruling) diluted in 100ml 0.9% N/S x IV x OD
11. With fever: Inj Paracetamol 1g/100ml (Provas) (SOS)
12. Inj Ceftriaxone 2g (Titan, Rocephin) dilute in 100ml 0.9% Normal saline x IV x once daily
 - Prophylactic antibiotics are not recommended, and should only be used in patients with evidence of infected necrosis
13. IV Pain management/analgesia:
 - ↳ Inj. Ketorolac 30mg/ml (Toradol) in 4–8ml 0.9% N/S x IV
 - ↳ OR Inj. Tramadol 100mg/2ml (Tramol) + Inj. Dimenhydrinate 50mg/ml (Gravinate) dilute in 100ml 0.9% NS. x IV
 - ↳ OR Inj. Nalbuphine 10mg/ml (Kinz) + Inj. Dimenhydrinate 50mg/ml (Gravinate) dilute in 100ml 0.9% NS. x IV

Opioids of choice is meperidine and morphine
14. With vomiting – consider ONE of the following anti-emetics:
 - ↳ Inj. Metoclopramide 10mg/2ml (Metaclo) x IV x TDS
 - ↳ OR Inj. Dimenhydrinate 50mg/ml (Gravinate) x IV x TDS
 - ↳ OR Inj. Ondansetron 8mg/4ml (Onset, Onseron) x diluted in 50 to 100 ml of 0.9% NS OR D5%W. IV over 15 minutes.



INTestinal Obstruction

△ Intestinal obstruction C/C:

- » Colicky abdominal pain
- » Obstipation/Constipation
- » vomiting &/or nausea
- » Abdominal distention
- » Increased high-pitched bowel sounds (early) or the absence of any bowel sounds (late) Diffuse abdominal tenderness
- » Collapsed, empty rectum on digital rectal examination (complete bowel obstruction); or impacted feces
- » History of abdominal surgery

Workup before operation

Send labs: CBC, Urea, creatinine & electrolytes, LFTs, PT & INR, Viral marker (Anti HCV, HBsAg)

Radiological Imaging:

Abdominal ultrasound: Multiple fluid-filled dilated bowel loops > 2.5 cm in diameter adjacent to collapsed bowel loops, Thickened bowel wall, and Prominent plicae circulares of dilated small bowel loops (referred to as the keyboard sign)

X-ray Chest PA view: Air under the diaphragm is an indicator of bowel perforation

X-ray abdomen Erect & supine view: Dilated bowel loops proximal to the obstruction, Rectal air shadow absent, Multiple air-fluid levels.

CT abdomen with IV and oral contrast: Similar findings as on x-ray, Transition point at site of obstruction

- » If Cardiac patient: ECG, and echocardiography

Indications of Immediate Surgery in Intestinal Obstruction:

- » Complicated bowel obstruction:
 - Signs of ischemia
 - Colonic perforation
 - Clinical deterioration
- » Obstructed or strangulated hernia
- » Operative decompression needed (in Toxic megacolon)
- » Volvulus of gut
- » Acute obstruction
- » Entero-lithotomy for gallstone ileus

Rx

1. Maintain ABCD&E
2. Admit the patient in surgical unit
3. No feeding by mouth (NPO-Bowel rest)
4. Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂.
5. Pass Nasogastric tube with continuous suction (in patients with persistent vomiting, significant upper GI distension, complete bowel obstruction, or volvulus) & Foley's catheterization for urine output
6. IV fluid therapy: Initial fluid resuscitation with 0.9% N/S, R/L, or Dextrose 5% followed by maintenance fluid therapy x IV x TDS
7. Correction of electrolytes imbalance
8. Consider IV empiric antibiotic therapy for intra-abdominal infection in complicated bowel obstruction.
 - » Inj. Metronidazole 500mg/100ml (Flagyl) x IV x TDS
 - » PLUS one of the following:
 - ✎ Inj. Ceftriaxone 1g (Titan, Rocephin) x IV x BD
 - OR Inj Cefuroxime 750mg (Zinacef, Zecof) x BD/TDS
 - OR Inj Ciprofloxacin 400mg/100ml (Novidate, Ciplet) x BD
- If Severe Infection Or High Risk Patient**
 - ✎ OR Inj Imipenem-Cilastatin 500mg-1g (Cilapen, Tienam) x TDS
 - OR Inj Meropenem 1g (Meronem, Meroget) x TDS
 - OR Inj Piperacillin-Tazobactam 4.5g (Tanzo, Tazocin EF) x TDS
9. Inj. Omeprazole 40mg (Ruling, Risek) diluted in 10ml 0.9% NS x IV x OD
10. IV analgesic for Abdominal Pain:
 - » Inj. Drotaverine 40mg/1ml (Nospa) x IV in 100ml 0.9% NS
 - » If pain not controlled give Inj. Ketorolac 30mg (Toradol, Ketor) in 4-8ml 0.9% N/S x IV. If the pain is more severe give Inj. Tramadol 100mg/2ml (Tramol) or Inj. Nalbuphine 10mg/1ml (Kinz)
 - PLUS with Inj. dimenhydrinate 50mg/1ml (Gravinate) dilute in 8ml 0.9% N/S or D/W x give slow IV (or dilute in 100ml 0.9% NS)
 - Note:** Opioids should be avoided in suspected paralytic ileus and acute colonic pseudo-obstruction.
11. With vomiting – consider ONE of the following anti-emetics:
 - ✎ Inj. Metoclopramide 10mg/2ml (Metaclon) x IV x TDS
 - ✎ OR Inj. Dimenhydrinate 50mg/ml (Gravinate) x IV x TDS
 - ✎ OR Inj. Ondansetron 8mg/4ml (Onset, Onseron) x diluted in 50 to 100 ml of 0.9% NS OR D5%W, IV over 15 minutes.

After complete workup transfer the patient to the operating room

Procedure: exploratory laparotomy

- ✎ Management of the obstruction (Adhesiolysis, hernia reduction, cecopexy, tumor resection)
- ✎ Resection of gangrenous bowel with restoration of intestinal transit or creation of a stoma.

SPONTANEOUS BACTERIAL PERITONITIS



Symptoms and signs of SBP may be subtle or absent.

- Diffuse abdominal pain/tenderness
- Fever and chills
- Worsening ascites
- New-onset or worsening encephalopathy
- Nausea, vomiting
- Constipation or diarrhea (peristaltic signs sparse or absent in cases of ileus)

Laboratory studies

- Blood cultures (2 sets)
- Inflammatory markers: ↑ CRP, ESR
- CBC: potentially leukocytosis
- LFTs, Serum albumin
- Viral marker (Anti HCV, HBsAg)
- Basic metabolic panel: to evaluate for acute kidney injury, hepatorenal syndrome, hyponatremia
- PT, APTT & INR
- Perform paracentesis without delay and before the administration of antibiotics.

Diagnostic paracentesis

Indications

Patients with cirrhosis and ascites with any of the following:

- Clinical deterioration or hospital admission
- Signs of infection (fever, hypothermia, tachycardia, tachypnea, shock, leukocytosis, acidosis)
- Gastrointestinal signs or symptoms (abdominal pain/tenderness, vomiting, diarrhea, ileus, GI bleed)
- Encephalopathy
- Worsening ascites
- Worsening liver and/or renal function

Peritoneal fluid analysis

- Neutrophil count is $\geq 250/\text{mm}^3$
- Bacterial cultures: often negative
- Albumin: serum-ascites albumin gradient (SAAG) > 1.1 indicates portal hypertension-related ascites.
- Total protein, glucose, LDH: helpful in distinguishing SBP from secondary bacterial peritonitis.

Ultrasound whole abdomen



- Maintain ABCD&E
- Pass Intravenous cannulation
- No feeding by mouth (NPO-Bowel rest)
- Perform a focused history and physical examination.
- Pass nasogastric tube and foley's catheterization
- Vitals monitoring: Check BP, PR, RR, Temperature, SpO2
- Bowel care: if constipation advice Syp. Lactulose/Skilex drop
- Start IV fluid therapy: Dextrose 5% or 10% 1L x IV x STAT
- Correction of electrolytes imbalance
- IV Inj. albumin supplementation
- Consider IV empiric antibiotic therapy for intra-abdominal infection in complicated bowel obstruction.
 - Inj. Metronidazole 500mg/100ml (Flagyl) x IV x TDS
 - PLUS, one of the following:
 - Inj. Ceftriaxone 1g (Titan, Rocephin) x IV x BD
 - OR Inj. Cefuroxime 750mg (Zinacef, Zecef) X BD/TDS
 - OR Inj. Ciprofloxacin 400mg/100ml (Novidate, Ciplet) X BD
- If Severe Infection OR High-Risk Patient
 - OR Inj. Imipenem-Cilastatin 500mg-1g (Tienam) X TDS
 - OR Inj. Meropenem 1g (Meronem, Meroget) X TDS
 - OR Inj. Piperacillin-Tazobactam 4.5g (Tanzo) X TDS
- IV analgesic for Abdominal Pain:
 - Inj. Drotaverine 40mg/1ml (Nospa) x IV in 100ml 0.9% NS
 - If pain not controlled give Inj. Ketorolac 30mg (Toradol) in 4-8ml 0.9% N/S x IV.
 - If the pain is more severe give Inj. Tramadol 100mg/2ml (Tramol) or Inj. Nalbuphine 10mg/1ml (Kinz)
 - PLUS, with Inj. dimenhydrinate 50mg/1ml (Gravinate) dilute in 8ml 0.9% N/S or D/W x give slow IV
- With vomiting – consider ONE of the following anti-emetics:
 - Inj. Metoclopramide 10mg/2ml (Metaclon) x IV x TDS
 - OR Inj. Dimenhydrinate 50mg/ml (Gravinate) x IV x TDS
 - OR Inj. Ondansetron 8mg/4ml (Onset, Onseron) x diluted in 50 to 100 ml of 0.9% NS OR D5%W, IV over 15 minutes.
- Inj. Omeprazole 40mg (Risek) diluted in 100ml 0.9% N/S x IV x OD
- Venous thromboembolism (VTE) prophylaxis: Inj. Clexane
- Inj. Paracetamol 1g/100ml (Provas) x SOS

❖ Identify and treat the underlying cause.



SECONDARY BACTERIAL PERITONITIS



Definition: inflammation of the peritoneum caused by bacterial infection from a surgically treatable intraabdominal source

- » Abdominal pain/tenderness
- » Peritoneal signs (e.g., local or diffuse rigidity, rebound tenderness, and/or guarding)
- » Gastrointestinal symptoms (e.g., nausea, vomiting, ileus)
- » Signs of infection (e.g., fever, tachycardia, tachypnea, hypotension, leukocytosis, sepsis, shock)
- » Worsening or lack of symptom resolution after initiation of antibiotics in a patient initially suspected of having SBP

Etiology

- » Perforation of an intraabdominal viscus (e.g., duodenal perforation due to a peptic ulcer).
- » Translocation of bacteria from an abdominal organ inflammation (e.g., appendicitis, diverticulitis, pancreatitis, intraabdominal abscess).
- » Trauma (e.g., penetrating wound)
- » Iatrogenic (e.g., surgery, anastomosis insufficiency, invasive procedure)

Send labs: CBC, Urea, creatinine & electrolytes, LFTs, PT & INR, Viral marker (Anti HCV, HBsAg).

Radiological tests:

- » Abdominal Ultrasound
- » Chest x-ray PA view
- » X-ray abdomen supine & erect view: Free air may be seen if viscous organ perforation is present.
- » CT scan of the abdomen and pelvis with IV contrast

Peritoneal fluid analysis

- » Neutrophil count is $\geq 250/\text{mm}^3$
- » Bacterial culture and/or gram stain: positive
- » Total protein $> 1 \text{ g/dL}$, LDH $>$ upper limit of normal for serum, glucose $< 50 \text{ mg/dL}$
- » Other: Carcinoembryonic antigen (CEA) $> 5 \text{ ng/mL}$ or alkaline phosphatase $> 240 \text{ U/L}$ suggests secondary peritonitis with intestinal perforation



1. Maintain ABCD&E
2. No feeding by mouth (NPO-Bowel rest)
3. Pass Nasogastric tube and Foley's catheterization
4. Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂
5. Bowel care: if constipation advice Syp. Lactulose/Skilex drop
6. Start IV fluid therapy: 0.9% N/S, R/L, &/or Dextrose 5% x IV stat
7. Correction of electrolytes imbalance
8. Consider IV empiric antibiotic therapy for intra-abdominal infection in complicated bowel obstruction.
 - » Inj. Metronidazole 500mg/100ml (Flagyl) x IV x TDS
 - » PLUS, one of the following:
 - ↳ Inj. Ceftriaxone 1g (Titan, Rocephin) x IV x BD
 - OR Inj. Cefuroxime 750mg (Zinacef, Zecef) x BD/TDS
 - OR Inj. Ciprofloxacin 400mg/100ml (Novidate, Ciplet) x BD
- If Severe Infection OR High-Risk Patient**
 - ↳ OR Inj. Imipenem-Cilastatin 500mg-1g (Cilapen) x TDS
 - OR Inj. Meropenem 1g (Meronem, Meroget) x TDS
 - OR Inj. Piperacillin-Tazobactam 4.5g (Tanzo) x TDS
10. Inj. Omeprazole 40mg (Risek) diluted in 10ml 0.9% N/S x IV x OD
11. IV analgesic for Abdominal Pain:
 - » Inj. Drotaverine 40mg/1ml (Nospa) x IV in 100ml 0.9% NS
 - » If pain not controlled give Inj. Ketorolac 30mg (Toradol) in 4-8ml 0.9% N/S x IV. If no improvement or severe pain give Inj. Tramadol 100mg/2ml (Tramol) OR Inj. Nalbuphine 10mg/1ml (Kinz) PLUS with Inj. dimenhydrinate 50mg/1ml (Gravinate) dilute in 8ml 0.9% N/S or D/W x give slow IV [or dilute in 100ml 0.9% NS]
12. IV antiemetics for vomiting as needed:
 - » Inj. Dimenhydrinate 50mg/1ml (Gravinate) x IV x TDS
 - OR Inj. Metoclopramide 10mg/2ml (Maxolon) x TDS (Risk of EPS)
 - » If no improvement than: Inj. Ondansetron 8mg/4ml (Onset, Onseron) - diluted in 50-100 ml 0.9% N/S over 15-20 minutes.
13. Inj. Omeprazole 40mg (Risek) diluted in 100ml 0.9% N/S x IV x OD
14. Venous thromboembolism (VTE) prophylaxis: Inj. Clexane x IM
15. With fever/analgesia: Inj. Paracetamol 1g/100ml (Provas) x SOS

After complete workup transfer the patient to the operating room
Procedure: exploratory laparotomy
 Secondary bacterial peritonitis usually requires imaging and urgent surgical management.

PRESSURE ULCER (DECUBITUS ULCER, BED SORE)

- Definition: Pressure ulcer is a focal area of unrelieved pressure resulting in ischemia, cell death, and necrotic injury of the epidermis and soft tissue due to prolonged pressure, also known as bed sores, or pressure ulcer, or decubitus ulcer or pressure sore or trophic ulcer or penetrating ulcer.
- Incidence: 5% of hospitalized patients; Higher incidence in: Paraplegic patients, elderly & severely ill patients
- Most common site: Ischium > Greater trochanter > Sacrum > Heel > Malleolus > Occiput
- Mechanism: External pressure exceeds the capillary occlusive pressure (>30 mm Hg) → Blood flow to the skin stops → Tissue hypoxia, necrosis and ulceration.
- Neurological Causes: Syringomyelia, Spina bifida, Spinal injury, Peripheral neuritis, Peripheral nerve injury, Leprosy, Diabetic neuropathy, Paraplegia and Tabes dorsalis
- Clinical Features: Painless punched out ulcer; Base formed by bone

STAGING OF PRESSURE ULCERS

Stage	Description
I	» Non-blanchable erythema without a breach in epidermis (early superficial ulcer)
II	» Partial thickness skin loss involving epidermis & dermis (Late superficial ulcer)
III	» Full thickness skin loss extending into subcutaneous tissue but not through underlying fascia (Early deep ulcer)
IV	» Full thickness skin loss through fascia with extensive tissue destruction, maybe involving muscle, bone, tendon or joint (Late deep ulcer)/The wound bed is fully covered with slough or eschar

Diagnostic workup

- Evaluate for predisposing factors, such as:
 - » Blood glucose level and HbA1C to assess for diabetes
 - » Serum albumin to assess for malnutrition
- Screen for complications
 - » CBC, CRP: Leukocytosis and ↑ CRP suggest an infectious complication.
 - » Wound swab: not routinely recommended; consider in patients with suspected MRSA infection
 - » Blood cultures: Consider in patients with deep ulcers and signs of sepsis.
 - » Radiology (x-ray, CT, or MRI): Consider if osteomyelitis or an underlying bony involvement is suspected.

Supportive care

- Redistribute pressure: Pressure relief over the affected or vulnerable area is one of the most important aspects of management.
 - » Immobile patients and patients with several or refractory ulcers:
 - » Frequent position changes (every 2 hours)
 - » Pad all pressure points.
 - » Alternating pressure mattress
 - » Mobile patients
 - » Optimize bedding with a foam mattress or overlay.
 - » Assist with movement for patients with limited mobility.
 - » All at-risk patients: pad pressure points on devices such as CPAP masks and physical restraints.
- Rigorous skin care
 - » Keep the skin clean and moisturized in order to prevent skin erosion and laceration.
 - » Advise caregivers to regularly inspect other at-risk areas to identify early stages of decubitus ulcers.
 - » Catheterization, bowel programs, and/or highly absorbent incontinence products (e.g., diapers, pads) may be helpful for patients with incontinence.
- Nutrition: Ensure adequate hydration and nutrition in all patients. Protein supplementation is recommended. Consider increasing daily calorie requirement and supplementing micronutrients to facilitate healing.

Wound management

- Cleaning

- ✎ Normal saline is a suitable cleaning agent.
- ✎ Limit the use of antiseptic fluids, because they inhibit the formation of granulation tissue.
- » **Dressings (e.g., hydrocolloids, foam dressings):** Perform frequently to absorb excess exudate while keeping the wound moist
- » **Debridement**
 - ✎ Used to remove devitalized tissue or biofilms to prevent or treat infection and enable healing
 - ✎ **Modalities:** sharp (surgical), mechanical, biological, enzymatic, and autolytic
 - ✎ In patients with suspected infection, obtain a swab or tissue for culture following debridement.
- » **Adjunctive treatment options:** electrical stimulation, negative pressure wound therapy, and administration of platelet-derived growth factor (**Negative pressure (vacuum-assisted) wound therapy:** A method of wound care management in which subatmospheric pressures are applied to a wound, increasing blood flow to the area and promoting accelerated wound healing).

Surgical management

- » **Surgical debridement, ulcer/eschar excision**
 - » Extensive ulcers with undermining of adjacent tissue, cavity formation, or large necrotic areas
 - » Management of associated infection (e.g., extensive cellulitis, abscess, or osteomyelitis)
 - » **Stage 3 or 4 wounds refractory to conservative management**
 - ✎ Deep ulcers (stage 3 or stage 4): patient unsuitable for surgery → debridement of necrotic tissue
 - ✎ Deep ulcers (stage 3 or stage 4): candidate for surgery → surgical debridement and reconstruction with flap formation
 - » **Secondary closure (e.g., tissue flap reconstruction):** clean, healing ulcers.
- N.B. Important consideration:** Conservative management may be more appropriate for patients who are not good candidates for surgery (e.g., multiple comorbidities, limited life-expectancy).



TREATMENT OF PRESSURE ULCER (DECUBITUS ULCER, BED SORE)

- ✎ **Prevention is the best treatment with:** Good skin care; special pressure dispersion cushions or foams; Use of low air-loss and airfluidized beds; Urinary or fecal diversion in selected case, bed bound patients turned at least every 2 hours
- ✎ Consult a wound care specialist, general surgery, and/or plastic surgery
- ✎ Wound hygiene, cleansing + dressing
- ✎ **Initiate treatment depending on the stage of the ulcer and whether an infection is present.**
 - » **Superficial, clean wound:** supportive care alone may be appropriate
 - » **Extensive and/or infected wound, wet eschar:** debridement, antibiotic therapy, and/or surgical management in addition to supportive care
 - » **Surgical treatment:** Reserved for the patient with no improvement after conservative management; includes adequate debridement, vacuum assisted closure or Flap closure
- ✎ **Initiate empiric antibiotic therapy:** for skin and soft tissue infections and adjust antibiotic therapy as needed
 - » **With mild infection:**
 - ✎ Mupirocin 2% topical ointment (Bactroban, Mupir) x topically on affected wound every 8 hours
 - ✎ OR Fusidic acid topical cream (Fucidin, Fuciderm) x topically on affected wound every 8 hours
 - » **with moderate infection:**
 - ✎ Cap. Clindamycin 300mg (Dalacin-C) orally 3-4 times daily
 - ✎ OR Cap. Cephalexin 500mg (Ceporex, Keflex) orally twice daily
 - ✎ OR Tab. Co-amoxiclav 625mg (Augmentin) orally 2-3 times daily
 - ✎ OR Cap. Doxycycline 100mg (Vibramycin) orally twice daily
- ✎ **Ensure adequate analgesia**
 - ✎ Tab. Paracetamol 500mg (Calpol, Panadol) 500-1000mg 3-4 times daily
 - ✎ OR Tab. Paracetamol 650mg + Orphenadrine 50mg (Neubrol fort) x three times daily
 - ✎ OR Tab. Diclofenac 50mg OR 75mg (Voren, Arnil) 50 mg x TDS or 75 mg x orally BD
 - ✎ OR Tab. Naproxen sodium 250mg OR 500mg (Flexin, Neoprox) 250-500 mg orally twice daily



DIABETIC FOOT INFECTIONS

Definition: The term "diabetic foot complications" encompasses the conditions of diabetic foot ulcer and diabetic foot infections. Diabetic foot complications, including ulcers and infections, are a common and costly complication of diabetes mellitus. The majority of diabetic foot ulcers are caused by repetitive trauma sustained during activity on a structurally abnormal, insensate foot. Ulcers act as a portal of entry for bacterial infections. Preventing and/or healing ulcers helps prevent infections and thereby minimizes risk of limb loss.

Etiology: Infections are typically polymicrobial. Staphylococci and streptococci spp. are the most common

Diabetic foot infections

C/C

Signs and symptoms

- » Edema
- » Induration
- » Erythema
- » Tenderness
- » Warmth
- » Purulent exudate

Classification of infection severity

- » **Mild:** superficial infection with ≤ 2 cm of erythema
- » **Moderate:** deep infection or > 2 cm of erythema
- » **Severe:** any degree of infection plus systemic inflammatory response syndrome

Diagnostic Workup:

- » CBC, CRP, ESR
- » Blood sugar level
- » Serum creatinine
- » Wound/discharge cultures via biopsy or curettage
- » X-ray foot
- » Arterial Doppler of the limb.
- » **Severe cases:** sepsis workup

If linezolid is not part of the regimen consider the addition of clindamycin to reduce the risk of TSS (antitoxin activity).



Rx

TREATMENT OF DIABETIC FOOT INFECTIONS

- » **Glycemic control:** by diet and using insulin therapy see T1DM & T2DM
- » Refer patients to a multidisciplinary foot care team when possible.
- » **Admit patients with any of the following criteria:**
 - » Severe infection or presence of systemic features (e.g., fever, nausea, vomiting, tachycardia, hypotension, uncontrolled hyperglycemia)
 - » Critical limb ischemia
 - » Barriers to follow-up
 - » Little response to outpatient management
 - » Traumatic or puncture wounds
- » **Wound care:** regular dressings that maintain a moist environment, including non-adherent dressings covered with a layer of gauze or other absorptive material, are generally best for wound healing.
- » **Initiate empiric antibiotic therapy:** for skin and soft tissue infections and adjust antibiotic therapy as needed based on culture results and continue for up to 4 weeks.
- » **Diabetic ulcer with mild infection:**
 - » **Cap. Clindamycin 300mg** (Dalacin-C) orally 3-4 times daily
 - » **OR Cap. Cephalexin 500mg** (Ceporex, Keflex) orally twice daily
 - » **OR Tab. Co-amoxiclav 625mg** (Augmentin) orally 2-3 times daily
 - » **OR Cap. Doxycycline 100mg** (Vibramycin) orally twice daily
- » **+ with moderate infection: add one of the following**
 - » **Tab. Levofloxacin 500mg** (Leflox, Cravit) once daily
 - » **OR Tab. Moxifloxacin 400mg** (Mofest, Moxiget) once daily
- » **Diabetic ulcer with moderate-severe infection/necrotizing infection**
 - » **Inj. Vancomycin 1000mg** (15mg/kg) twice daily x IV x twice daily
 - » **OR Inj. Linezolid 600mg/300ml** (Ecasil, Nezkil) x IV x BD
 - » **PLUS one of the following**
 - » **Inj. Piperacillin/tazobactam 4.5g** (Tanzo, Tazocin) x TDS
 - » **OR Inj. Meropenem 1g** (Meronem, Penro) x IV x TDS
 - » **OR Inj. Moxifloxacin 400mg/250ml** (Mofest, Moxiget) x IV x OD
- » **After initial treatment:**
 - » Follow up and continuing diabetic care $\pm$ referral to specialist
 - » **Surgical debridement:** Necrotic tissue must be judiciously debrided. In some cases, resection of the underlying bony prominence may improve wound healing.
 - » **Mechanical offloading:** fitting of therapeutic footwear or total contact cast. Microcellular rubber (MCR) shoes to prevent injuries; care of foot.
 - » **Endovascular intervention and/or surgical bypass** in patients with underlying PAD to establish adequate arterial perfusion to the foot.
 - » **Amputation:** Minor amputation (i.e., toe or partial-foot resections), major amputations: Extensive infection or gangrene that reconstruction either is not possible or will not preserve meaningful function in affected limb or in patients who have very little or no function in the affected limb



HYPERTROPHIC SCAR

- Definition: cutaneous condition characterized by high fibroblast proliferation and collagen production that leads to a raised scar that does not grow beyond the boundaries of the original lesion.
- Causes: imbalance in wound healing processes due to local factors and genetic factors
- Clinical presentation: onset ≤ 3 months, raised, red or flesh-colored scar that does not grow beyond the boundaries of the original scar, possibly erythematous, firm, pruritus and painful
- Pathophysiology: threefold increase in the synthesis and parallel deposition of collagen type-III, Results from prolonged inflammatory phase of wound healing and/or unfavorable scar citing (across the lines of skin tension)
- Histology
 - » Excess collagen and hypervascularity (more marked in keloid with more type-III collagen)
 - » Contains well organized type III collagen; Improves spontaneously with time
- Diagnosis: based on clinical appearance of lesion and patient history of trauma or surgery
- Prevention: follow surgical principles associated with decreased risk of scar development (e.g., incisions should follow skin creases to reduce tension on the suture)
- Prognosis: Frequently regress within 1 year without treatment. Typically respond well to treatment, if needed

TREATMENT OF HYPERTROPHIC SCAR

Medical treatment (first line):

(Avoid silicon in open wounds)

- » Linear hypertrophic scar: Silicone scar gel or sheets x Apply to the affected area x BD for atleast 3 months.
- » Ongoing hypertrophic scar: Intralesional corticosteroids injection
 - » Inj. Triamcinolone 40mg/ml (K-Cort, Kenacort) after cleaning the skin with an alcohol wipe, 10mg/ml is injected into the lesion/scar using an insulin syringe and 25-gauge needle.
 - » Consider lidocaine to the steroid to give a 50/50 dilution
 - » Typically administered every 2 to 4 weeks for ≤ 6 months
 - » Decreases scar thickening, and relieves pain and pruritus, if present.
 - » Contraindications: active infection at scar site, allergy
 - » Adverse effects: Hypopigmentation or hyperpigmentation, skin atrophy, telangiectasias, pain

- » Pressure therapy: Pressure may work by causing local tissue hypoxia.

Options: Referral for custom fitting may be required.

- Pressure clips for the earlobes
- Compressive masks for the face
- Garments or bandages (spandex, elastic adhesive) for the body

Instructions for use: Wear 23 hours a day with a pressure of 24-30mmHg.

Contraindications: severe PAD, decompensated CHF

- » Surgical excision: Consider only after trialing all other first-line treatments

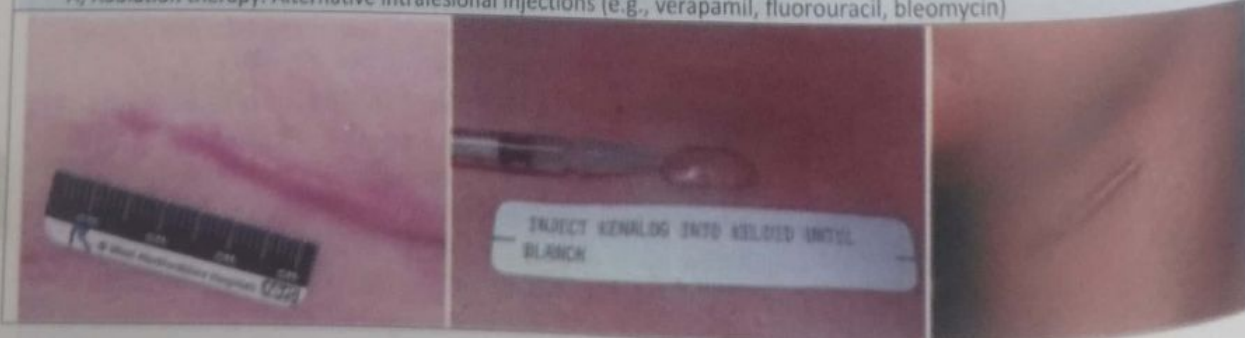
- Linear or widespread hypertrophic scars present > 6 months after injury if causing functional impairment
- Any hypertrophic (or keloid) scars present > 12 months after injury (Scar persist after 1 year)

Options: 1. Partial or complete removal of the scar with primary wound closure, 2. Skin graft or flaps for scar contractures

- » Additional therapies (May be used in combination with first-line therapies to improve outcomes by specialist):

Cryotherapy, corticosteroid tape, photodynamic therapy, laser therapy (e.g., pulsed dye laser), Imiquimod, Botulinum toxin A, Radiation therapy. Alternative intralesional injections (e.g., verapamil, fluorouracil, bleomycin)

Lidocaine has a local anesthetic effect but will not reduce the pain of the injection (though it may make the subsequent pain more tolerable). Of more significance, though, is that lidocaine has local effects on fibroblasts, causing reduced collagen production and inhibiting cell



KELOIDS

- Definition: skin lesions caused by high fibroblast proliferation and collagen production as excessive tissue response to, typically small, skin injuries
- Etiology: Unknown; imbalance in wound healing processes due to local factors, Genetic predisposition, more common in blacks/darken skin types
- Pathophysiology: 20-fold increased synthesis and unorganized deposition of type-I collagen and type-III collagen and fibroblast proliferation
- Associated with: Elevated levels of growth factors; deeply pigmented skin
- Common in certain areas of body: Above clavicle, upper extremities, on the trunk, face (Especially seen in triangle whose boundaries are xiphisternum and each shoulder tip)
- Histology
 - Excess collagen & hypervascularity; Contain disorganized type I & III collagen
 - Thicker collagen bundles form acellular node like structures
- Clinical course: No spontaneous regression. Recurrence is frequent after surgical excision.

△ Keloids C/C:

- Onset: ≥ 3 months
- Thickened, Brownish-red scar tissue of varying consistency (soft or hard) with claw-like appearance, irregular scar that grows beyond the boundaries of the original scar
- Pruritus, Pain
- Localization: Can occur anywhere; most commonly seen on earlobes, face (especially cheeks), upper extremities, chest, pubic area

Keloid scars extended beyond the wound edges, while hypertrophic scars remain within.

Diagnosis: based on clinical appearance of lesion and patient history of trauma or surgery

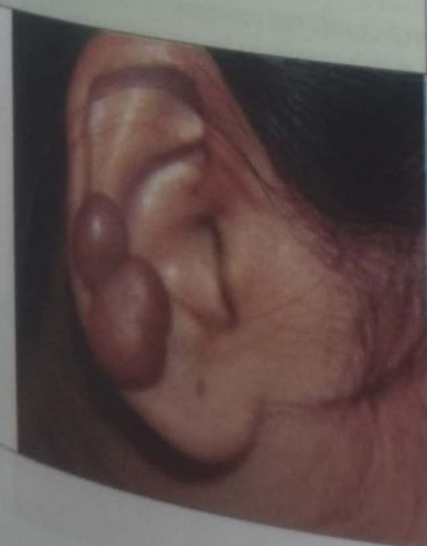
Rx

TREATMENT OF KELOIDS SCAR

- Treatment option same as Hypertrophic scar
- Keloids rarely regress with time, often refractory to medical and surgical intervention.
- First line treatment: Silicones gel in combination with pressure therapy and intralesional corticosteroid injection
See treatment of hypertrophic scar
- Refractory cases (after 12 months of therapy): Excision + Post-op radiotherapy (external beam or brachytherapy)
- New treatment modalities: Internal cryotherapy and 5% Imiquimod

Prognosis

- Respond better to early treatment.
- Flatten after treatment with intralesional corticosteroid injections in up to 50% of cases.
- Nearly always recur after surgical excision unless other therapies are also administered.



LIPOMA

- Definition: most common benign tumor of subcutaneous soft-tissue. Can be encapsulated or diffuse, it is also known as universal tumor.
- Etiology: Unknown, genetic predisposition
- Pathology: Lobulated tumor made up of mature fat cells
- Special type of lipoma: Lipomatosis is an autosomal-dominant disorder characterized by multiple lipomas

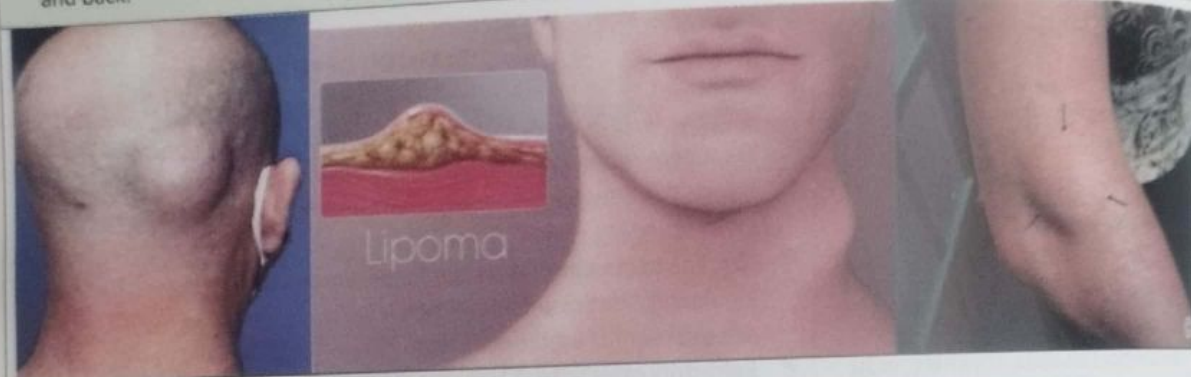
Clinical features:

- » Diagnosis is clinical.
- » Slow-growing round, soft, rubbery tumor (may be solitary or multiple).
- » Typically non-tender, soft and fleshy on palpation
- » May grow to a large size and become substantially deforming.
- » Localization: typical locations are head, neck, shoulders, and back.

Rx

TREATMENT OF LIPOMA

- » Treatment of lipoma usually not required.
- » Surgical Excision of the LIPOMA, can be considered in the following cases:
 - » If tumor causes pain
 - » Cosmetic reasons
 - » If tumor grows rapidly or is firm on palpation



SKIN TAG (ACROCHORDON)

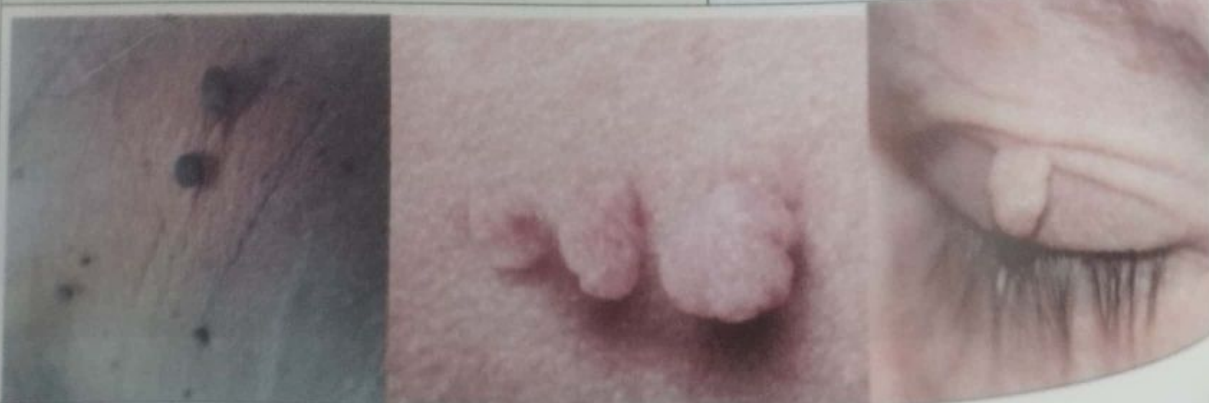
- Definition: small, papillomatous skin lesions that most commonly arise in skin creases
- Etiology: Not fully understood; thought to be caused by frequent irritation, e.g., skin rubbing on skin
- Association: Associated with HPV and endocrine changes; (e.g., during pregnancy, or in obesity, type 2 diabetes mellitus, and acromegaly), Perianal acrochordons are associated with Crohn disease.
- Histopathology: composed of hyperplastic epithelium & accumulations of collagen; usually well-vascularized
- Differential diagnoses: warts, seborrheic keratosis, neurofibromas, nevi, basal/squamous cell carcinoma

Clinical features:

- » Diagnosis is clinical.
- » Typically arise in locations exposed to friction; (E.g., lower neck, axilla, inframammary fold, inguinal region)
- » Usually small, soft, sometimes slightly discolored, pedunculated outgrowths with a smooth surface
- » Localization: typical locations are head, neck, shoulders, and back

Rx

- » Treatment usually not required.
- » Skin tag may be removed for cosmetic reasons.
- » Removal methods include surgical excision (usually with fine-grade scissors), cryotherapy, and electrodesiccation.



GANGLIONIC CYST

Introduction: Ganglion cysts are the most common benign lesion of the hand/wrist. Typically, insidious onset with no predisposing conditions. Usually only a cosmetic problem but local pain and neurovascular compression may occur. Ganglion cysts are usually diagnosed clinically without the need for further laboratory or imaging studies unless other pathological processes are suspected. Conservative management usually suffices if no neurovascular compromise. 38-58% cysts can disappear without any treatment at all. Aspiration of dorsal cysts can be therapeutic and diagnostic. Surgical excision has a higher rate of resolution, but recurrence is possible.

Clinical features: (Clinically diagnosis)

- » Subcutaneous wrist mass, non-tender mass, Increased mass size after activity
- » Wrist pain
- » Transilluminating mass
- » Hand or finger coolness
- » Numbness/weakness of fingers/hand.

TREATMENT OF GANGLIONIC CYST

First line treatment:

Observation or conservative measures include:

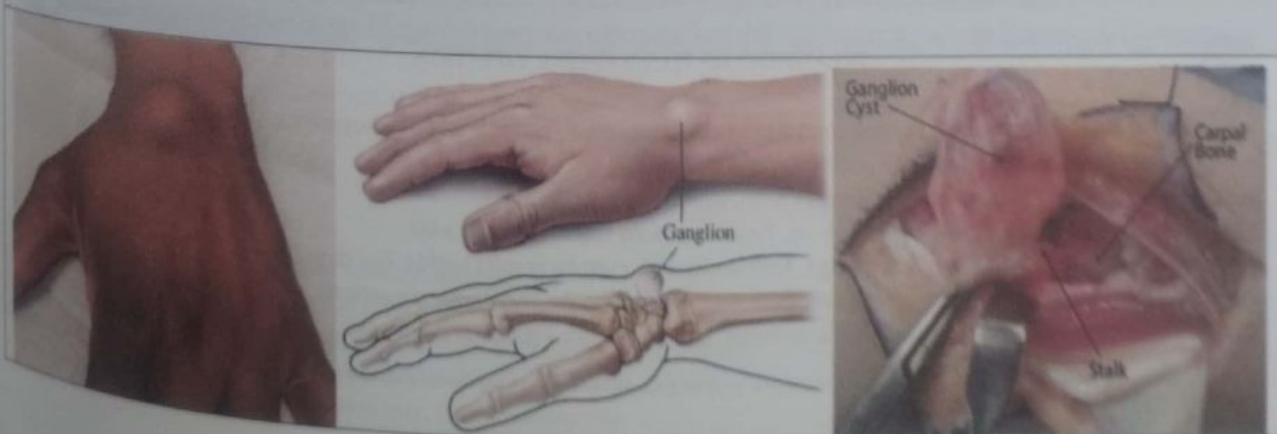
- » Activity modification to avoid painful wrist positions or volar wrist splinting for pain control.
- » Conservative treatment can lead to spontaneous resolution in up to 58% of adults and up to 93% of children over a 9 to 12-month period.
- » Analgesia if activity related pain/discomfort:
 - » Tab. Naproxen 250-500 mg (Flexin, Neoprox) x orally BD when required, maximum 1250 mg/day
 - » Tab. Diclofenac potassium 50mg (Voren, Voltrel) 2-3 times daily when required, maximum 150 mg/day
- » Consider gastro-protective: Cap. Esomeprazole 40mg (Esso, Eskem) x Once daily.
- » Antibiotics are not recommended. Antibiotic prophylaxis for procedures or partial infection only.

2nd line treatment: Cyst aspiration ± corticosteroid injection.

- » Inj. Triamcinolone 40mg/ml (K-Cort, Kenacort) x 10mg into the affected area as a single dose.
- » AND Inj. Lidocaine 1% x 1-2 mL into the affected area as a single dose.
- » Cyst puncture and drainage if no neurovascular comprises cyst.
- » Volar ganglion cysts aspiration is not recommended due to the potential risk of injury to the radial artery.

3rd line treatment: Surgical Excision

- » Cysts that are recalcitrant to conservative management may be addressed surgically if they are painful or cosmetically displeasing and the patient desires excision of the mass.
- » Surgery is recommended as a first line treatment when there are paresthesias, muscle weakness, or vascular insufficiency.
- » Prior to surgery patients should be advised that they will be trading cosmetic masses for surgical scars, and that complete excision may be prevented if the cyst encapsulates neurovascular structures.
- » Patients with neurovascular compromise related to ganglia are typically treated with surgical resection.



INGROWN TOE-NAIL

- Definition: abnormal growth of the nail plate into the lateral periungual skin, resulting in an inflammatory foreign body reaction with the risk of subsequent infection. More common in male than female (2:1).
- Etiology/Risk factors:
 - » Extrinsic risk factors: improper nail trimming (most common), tight-fitting shoes, repetitive trauma, hyperhidrosis, and certain medications (e.g., EGFR inhibitors).
 - » Intrinsic risk factors: abnormal nail shape and other anatomical abnormalities.
 - » Secondary bacterial infection is most frequently caused by *Staphylococcus aureus*.
- Pathogenesis: excessive nail trimming → formation of a spicule that pierces the lateral nail sulcus → inflammatory foreign body reaction → granulation tissue and disruption of the cutaneous barrier → infection.
- Clinical features: The hallux toenails are most commonly affected. Inflammatory signs with difficulty walking. Hypertrophic granulation tissue. Abscess formation and purulent drainage in case of secondary infection.

TREATMENT OF INGROWN TOENAIL

- Rx**
- Preventive treatment: Adequate trimming of the nails, proper footwear, and good foot hygiene.
- Conservative treatment: For lesions with mild inflammatory signs, Placement of different materials (cotton, gutter) under the ingrown nail plate to reduce the contact between the nail plate and the nail fold.
- Surgical treatment:
 - » For recurrent, infected, or ingrown nails with severe inflammation or in failure of conservative measures
 - » Partial nail avulsion or complete nail excision
 - » Antibiotics therapy are NOT RECOMMENDED unless cellulitis occurs (same as below - Felon finger).

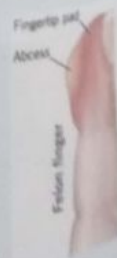


FELON FINGER INFECTION

- Definition: subcutaneous infection of the distal digital pulp. **Most common pathogen:** *Staphylococcus aureus*
- Etiology: Trauma with secondary infection, Progression of untreated paronychia. **Pathophysiology:** fingertip puncture wound → bacterial inoculation → closed-space infection of the digital pulp → ischemic necrosis
- Clinical features: Diagnosis is clinical, commonly affects the thumb or index finger. Signs of acute inflammation (e.g., warmth, redness). Tense swelling confined to the digital pulp. Progressive, severe throbbing pain exacerbated by the dependent position. Fluctuance and spontaneous drainage.
- Diagnostic workup: Soft tissue ultrasound if an abscess is suspected. Consider x-rays to evaluate for retained foreign bodies. Bacterial culture of drained fluid or pus if felon incision and drainage is performed.

TREATMENT OF FELON FINGER INFECTION

- Rx**
- Initiate oral antibiotics with *S. aureus* coverage: Tab. Amoxicillin/clavulanate 1g (Augmentin, Calamox) x BD OR Cap. Cephalexin 500mg (Ceporex, Keflex) x BD/TDS.
- Analgesia: Tab. Diclofenac sodium 50mg (Voren, Voltral) x BD/TDS
- Tetanus-prone wounds: prophylaxis with Inj. Tetanus toxoid 0.5ml (Imatet) x IM
- Abscess present: Felon incision & drainage. Follow-up with culture results within 2–3 days.
- Abscess absent: conservative management with warm water soaks and digital elevation
- Complications: Soft tissue necrosis, Septic arthritis, Osteomyelitis, Flexor tenosynovitis



ACUTE PARONYCHIA

- Definition:** Acute paronychia is the inflammation of the proximal and/or lateral nail folds of the fingers or toes for < 6 weeks. Most commonly caused by a bacterial infection (e.g., with *Staphylococcus aureus*).
- Pathophysiology:** trauma to the nail folds (e.g., due to manual work, nail biting, a manicure) → disruption of the barrier between the nail plate and the nail fold → increased susceptibility to bacterial infection.
- Clinical features:** Diagnosis is clinical. Usually involves only one digit. Signs of acute inflammation (e.g., redness, warmth). Skin abscess may be present. Absence of nail changes.
- Diagnostic workup:** If an abscess is suspected – soft tissue ultrasound, digital pressure test

TREATMENT OF ACUTE PARONYCHIA

- Treatment of MILD ERYTHEMA without abscess:**
 - Warm water soaks for 15 minutes 2–4 times per day.
 - Topical antibiotics (Off-label): Mupirocin 2% ointment (Bactroban, Mupir) OR Fusidic Acid 2% cream (Fudic, Fucidin) OR Fusidic Acid + Hydrocortisone (Fudic-H, Fucidin-H) x Twice daily for 7–10 days
- Treatment of acute paronychia with abscess formation:**
 - Perform acute paronychia incision and drainage.
 - Obtain informed consent.
 - Soak the digit to soften the eponychium.
 - Perform a digital block with 1% lidocaine (Xylocaine) as required.
 - Using a sharp instrument (e.g., No. 11 blade scalpel, needle tip), lift the eponychium away from the nail matrix.
 - Keep the instrument parallel to the nail and continue to lift the eponychium around the border of the paronychia until all of the pus has been released.
 - Apply antibiotic ointment and an absorbent dressing.
 - After the procedure, initiate oral antibiotics with *S. aureus* coverage: Tab. Amoxicillin/clavulanate 1g (Augmentin, Calamox) x BD OR Cap. Cephalexin 500mg (Ceporex, Keflex) x BD/TDS OR Cap. Clindamycin.
- Tetanus-prone wounds:** prophylaxis with Inj. Tetanus toxoid 0.5ml (Imatet) x IM
- Complications:** Felon, Osteomyelitis, Chronic paronychia



CHRONIC PARONYCHIA

- Definition:** inflammation of the proximal and/or lateral nail folds of the fingers or toes for > 6 weeks. Most common in occupations with repeated exposure to moisture and/or skin irritants (e.g., bartenders, dish cleaners). Most commonly caused by chronic exposure to skin irritants (e.g., household chemicals), rarely caused by infections.
- Pathophysiology:** disruption of the barrier between the nail plate and the nail fold (e.g., due to trauma, skin irritants) → persistent exposure of the nail fold to skin irritants → eczematous inflammatory reaction.
- Clinical features:** Diagnosis is clinical. Usually involves more than one digit. Dystrophic nails (e.g., thickened, discolored). Retraction of the proximal nail fold and loss of the cuticle. Signs of acute inflammation (e.g., redness, warmth). Abscess rare

TREATMENT OF CHRONIC PARONYCHIA

- Treatment of MILD ERYTHEMA without abscess:**
 - Avoid skin irritants and keep the area dry.
 - Apply a topical antiinflammatory agent: Triamcinolone OR Tacrolimus
- Patients with refractory chronic paronychias, Refer to hand surgery.
- Complications:** Nail dystrophy, Nail loss, Acute paronychia



HORDEOLUM (STYE)

Common acute inflammation of the tear gland or eyelash follicles (Zeis or meibomian glands)

Etiology

- » Mainly *Staphylococcus aureus*, rarely *Streptococcus*
- » Increased occurrence in individuals with acne vulgaris and diabetes mellitus

Classification

- » **External hordeolum:** inflammation of Moll's or the Zeis gland at the lid margin
- » **Internal hordeolum:** inflammation of the meibomian gland; usually visible at the palpebral conjunctiva (less common)

△ HORDEOLUM (STYE)

C/C:

- » Painful
- » Erythematous
- » Tender pus-filled nodule
- » Spontaneous perforation and purulent discharge after a few days

Rx

- » Most are self-limiting and resolve spontaneously after 1–2 weeks.
- » Warm compress and massage
- » Eyelid margin hygiene
- » Topical antibiotics

In the case of non-response to medical therapy or severe symptoms: incision and curettage, with systemic antibiotics (e.g., cephalexin)

CHALAZION (MEIBOMIAN GLAND LIPOGRANULOMA)

Chalazion is an acute or chronic inflammation of the eyelid secondary to blockage of one of the meibomian or Zeis oil glands in the tarsal plate

Etiology

- » Poor eyelid hygiene, stress, or immunodeficiency
- » **Systemic conditions:** tuberculosis, rosacea, seborrheic dermatitis
- » **Local anatomical abnormalities:** complications of chronic blepharitis, malignancy, eyelid trauma, or post-surgery

△ HORDEOLUM (STYE)

C/C:

- » Chronic (slow-growing)
- » Firm, rubbery nodule on the eyelid
- » Heaviness of the eyelid
- » Can cause visual disturbances, if large enough

Diagnosis:

- » Usually a clinical diagnosis → Everting the eyelid may allow for better visualization of the lesion.
- » **Biopsy:** for a persistent or recurrent chalazion, may be a sign of a sebaceous carcinoma (a carcinoma of the meibomian gland). Chalazion may also clinically resemble a basal cell carcinoma (BCC)

Rx

1. Conservative:

- » Wait and watch
- » warm compresses
- » Eyelid hygiene

2. In secondary infection: local antibiotics, e.g., tetracycline, doxycycline, minocycline, or metronidazole

» Chronic or recurrent chalazia may require

- » Incision and curettage/drainage depending on the size
- » Intralesional steroids - injection of corticosteroids into the lesion or incision

- » Refer to an ophthalmologist in 1 to 2 weeks.



IRITIS (ANTERIOR UVEITIS)

- It is also called anterior uveitis → inflammation of the uvea
- Uveitis is often associated with HLA-B27 syndromes, such as Crohn disease, ulcerative colitis, ankylosing spondylitis, psoriatic arthritis, juvenile idiopathic arthritis, and reactive arthritis.

△ Iritis (Anterior Uveitis)

C/C:

Diagnosis:

- » History: Nil or other inflammatory disease
- » Sensation: Pain, photophobia
- » Vision: Decreased
- » Discharge: Tearing
- » Pupillary Right Reflex (PLR): Normal
- » Conjunctival injection: Circumcorneal
- » Corneal appearance: Keratic precipitates
- » Intraocular Pressure (IOP): Normal/Elevated

Diagnostics

- » Diagnosis is made with slit lamp examination
- » Conjunctival smear and cytology if infectious cause is suspected
- » Tonometry
- » Further workup of any suspected underlying systemic condition

Rx

OPHTHALMIC REFERRAL

For Knowledge Purpose

Initial treatment

1. Topical Glucocorticoids.
2. Topical Cycloplegics: e.g., atropine, scopolamine
3. Analgesics: e.g., NSAIDs (Voren)
4. Close followup examinations

- » Infectious uveitis: antibiotic or antiviral therapy
- » Severe cases or those resistant to initial treatment
 - Systemic glucocorticoids
 - Immunosuppressant's (e.g., azathioprine, cyclosporin, infliximab)

ACUTE MUCOPURULENT CONJUNCTIVITIS

- Common acute inflammation of the tear gland or eyelash follicles (Zeis or meibomian glands)
- The most common type of bacterial conjunctivitis. Most common causative organism is staphylococcus aureus, other are Hemophilus aegyptius, pneumococcus, strep pyogenes, gonorrhea and H. Influenza.
- Perform fluorescein stain of the cornea (especially in infants) to avoid missing a corneal abrasion, ulcer, or herpetic dendrite.
- Consider culture and sensitivity of the discharge in severe cases and give antibiotics accordingly.
- Cases are frequently self-limited, but antibiotic treatment shortens course of symptoms.

△ Bacterial conjunctivitis

C/C:

- » Eye discomfort
- » Foreign body sensation
- » watering of the eye
- » Mucopurulent discharge
- » Sticking together of lid margins with discharge during sleep.
- » Slight blurring of vision sometimes color halos.

On P/E:

- » Conjunctival congestion
- » Chemosis: swelling of conjunctiva
- » Pneumococcal conjunctivitis: Petechial hemorrhage

Rx

1. Irrigation of conjunctiva to remove excessive discharge may be useful in hyperpurulent cases
2. Wearers of soft contact lenses: should be discontinued until at least 48 hours after complete resolution of symptoms
3. Risk of transmission should be reduced by hand-washing and the avoidance of towel sharing.
4. Topical antibiotics
 - » Ciprofloxacin 0.3% eye drops (Ciloxan, Ethiflox, Rocip) 1-2 drops in affected eye every 2 hour, while awake x 2 days
Than 1-2 drops 4 hourly for 5 days
OR Moxifloxacin 0.5% eye drops (Moxiral, Moxigan, Megamox) x 1 drop in affected eye for 2-3 days if not improved than 5 days
 - » ± Tobramycin eye ointment (Tobrex, Nebra) 2 times a day in affected eye. (if severe than 3 times/day)

CHLAMYDIAL CONJUNCTIVITIS

- Common cause of prolonged red eye due to inflammation of the eyelash follicles along the edge of the eyelid.
- The most common cause Chlamydia trachomatis
- In a patient with adult chlamydial conjunctivitis, other sexually transmitted infections should be excluded.
- Transmission is by autoinoculation from genital secretions, although eye-to-eye spread probably accounts for about 10%. The incubation period is approximately a week.

△ Chlamydial Conjunctivitis

C/C:

- Redness of eye (U/L or B/L)
- Watery or mucopurulent discharge
- Superficial punctate keratitis is common
- Large follicles are often most prominent in the inferior fornix and may also involve the upper tarsal conjunctiva
- Eye Pain, Itchiness
- Foreign body sensation
- watering of the eye
- Photophobia, blurred vision

Rx

1. **Tab. Azithromycin 500mg** (Azitma, Zetro, Macrobac)
1g (2 tablets) as single dose or maybe repeated after 1 week
is generally the treatment of choice
OR **Cap. Doxycycline 100 mg** (Vibramycin, Doxyn)
1-0-1 (Twice daily) for 7-10 days
2. **Topical antibiotics**
↳ **Tetracycline 1% eye ointment** (Ophth-Tetracyl, Novocin)
Alternative: Erythromycin 1% eye ointment

ALLERGIC CONJUNCTIVITIS

- Airborne allergen interacts with IgE within the eye, leading to mast cell degranulation

△ Allergic Conjunctivitis

C/C:

- Bilateral symptoms
- General signs and symptoms of conjunctivitis.
- Sneezing
- Itching

Diagnosis:

- History:** Hay fever, asthma, eczema
- Sensation:** itching of eye
- Vision:** Normal
- Discharge:** Mucous
- Pupillary Right Reflex (PLR):** Brisk
- Conjunctival injection:** diffuse
- Corneal appearance:** Diffuse, tarsal cornea
- Intraocular Pressure (IOP):** Normal

Rx

- Avoid chronic irritation (contact lenses, allergens avoidance)
- Cold compresses**
- If indicated:**
 - » If eye pain → **Ketorolac 0.5% eye drops** (Ketrosan, Ketrol)
 - » **Artificial tear eye drops** (Tear plus, Optitears, Visol gel)
- 1. **Olopatadine hydrochloride eye drops** (Olopat, Patanol)
1 drop two times a day.
Maximum treatment duration: 4 months
- 2. **Systemic anti-allergic:** If any symptoms of allergy
Tab. Cetirizine 10mg (Rigix, Zyretic)
OR **Tab. Loratidine 10mg** (Softin, Lorin-NSA)
OD/BD
- Alternative anti-allergic eye drops:**
Naphazoline hydrochloride 0.025% eye drops (Curine)
OR **Naphazoline hydrochloride 0.1% eye drops** (Naphcon Forte)
OR **Naphazoline HCL + Pheniramine maleate** (Nafamine)



VIRAL CONJUNCTIVITIS (ADENOVIRUS CONJUNCTIVITIS)

- Non-specific acute follicular conjunctivitis most common type of conjunctivitis.
- Epidemic keratoconjunctivitis ("Pinkeye") is a more severe type of adenovirus infection that is highly contagious and tends to occur in epidemics.
- Transmission: direct contact, fecal-oral route, or contaminated water (e.g., swimming pools)
- Etiology: Adenoviruses (most common), herpes simplex virus (HSV), varicella-zoster virus (VZV), picornavirus, molluscum contagiosum, HIV (highly contagious), measles, zika
- Slit lamp examination demonstrates follicles (small, regular, translucent bumps) on the inferior palpebral conjunctiva. Punctate fluorescein staining represents keratitis. Make sure to examine the cornea with fluorescein to avoid missing a herpetic dendrite.
- Conjunctival smear and cultures, viral isolation, or PCR if symptoms are recurrent/chronic
- A 'point-of-care' immunochromatography test takes 10 minutes to detect adenoviral antigen in tears; sensitivity and specificity are excellent.

△ Non-specific acute follicular conjunctivitis

C/C:

- » Frequently associated with exposure to an infected person or recent upper respiratory infection (sore throat or common cold).
- » Red eye with itching
- » Burning, or a foreign body sensation
- » Watery to mucous discharge
- » Generally, one eye will be involved initially, with the other eye becoming involved within several days later.
- » There is no eye pain unless there is some degree of keratitis.

Physical examination:

- » U/L or B/L conjunctival injection
- » Chemosis (swelling of the conjunctiva)
- » Small subconjunctival hemorrhages
- » Preauricular lymphadenopathy.



Rx

Treatment of Viral conjunctivitis

Safety Precautions/General instruction

- » Viral conjunctivitis can take 1 to 3 weeks to run its course. It is highly contagious and great care should be taken to prevent transmission of the disease.
- » Reduction of transmission risk by meticulous hand hygiene with handwashing with soap & water for at least 20 seconds, avoiding eye touching or rubbing.
- » Avoid sharing personal items: Pillows, glasses and towels
- » Cool compresses gently applied around the eye area
- » Wearers of soft contact lenses (Grey glasses)

1. **Topical antihistamine/decongestants** (Naphcon-A, Ocucon-A)
Naphazoline + Pheniramine maleate Eye Drops x 1-2 drop 3 to 4 times daily as needed for redness & conjunctival congestion
2. **If dry eye: Artificial tears eye drops** (Tear plus, Systane)
One drop 5-6 times a day.
3. **For secondary bacterial cause**
 - ↳ Tobramycin 0.3% eye drops (Tobrex, Nebra) x 1 - 2 drop in affected eye for every 4 - 6 hour.
 - ↳ Moxifloxacin 0.5% eye drops (Moxigan, Moxiral) x 1 drop in affected eye for 2-3 days if not improved than 5 days.
- ❖ It is Self-limiting condition and do not need treatment with an antimicrobial ocular agent. Use if any secondary infection.
- ❖ Steroid eye drops are contraindicated except under the strict supervision of an ophthalmologist.

HERPES SIMPLEX KERATITIS

Herpes simplex keratitis (viral keratoconjunctivitis) usually presents initially as an infection of the epithelial cell layer, although with recurrent episodes, stromal involvement may be seen. It is most often a unilateral infection. As with other herpetic infections, it is not possible to eradicate the virus, but limitation of inflammatory-mediated damage is important.

Etiology: Most common cause is herpes simplex virus-1 (HSV-1) → ocular exposure to viral-laden lesions → HSV-1 enters sensory nerve endings and lays dormant in the trigeminal nerve ganglion.

Slit-lamp examination: corneal dendritic lesions on slit-lamp examination with fluorescein

△ Herpes simplex keratitis

C/C:

- » Patients complain of a scratchy
- » Foreign body sensation,
- » Eye pain, Redness, watering
- » A variable decrease in visual acuity.
- » Usually affects one eye; may be bilateral, especially in severely atopic patients
- » Photophobia

Diagnostic & Evaluation: Workup of HSV keratitis proceeds in the following manner

- » **History:** It is the first step to pinpoint the etiology of the disease.
- » **External examination:** Distribution of skin vesicles may help distinguish HSV (vesicles concentrated around the eye) from HZV (vesicles extended to the forehead, scalp, and tip of the nose) keratitis.
- » **Slit-lamp examination:** The most important step since it helps identify the characteristic signs of herpes keratitis. The ulcer bed is visualized better with fluorescein dye while the virus-laden cells at the margins with rose bengal dye.
- » **Check corneal sensation:** This may decrease in herpes keratitis. Do this before instilling topical anesthetic.
- » **Laboratory tests:** Herpes simplex is usually diagnosed clinically and requires no laboratory confirmation. If the diagnosis is in doubt, any of the following tests are options:
 - » Scrapings of a corneal or a skin lesions for Giemsa stain or Tzanck smear - ELISA testing is also available
 - » Viral culture
 - » HSV antibody titers. They rise after primary but not recurrent infection

Rx

Precautions/General measure

- » Viral conjunctivitis is highly contagious and great care should be taken to prevent transmission of the disease.
- » Herpes simplex virus (HSV) conjunctivitis is usually self-limiting, but may need treatment with topical or oral antivirals in more severe disease, particularly if corneal involvement is suspected.
- » Reduction of transmission risk by meticulous hand hygiene, avoiding eye rubbing and towel sharing.
- » Instruct the patient to wash hands frequently and use separate towels.
- » **Cool compresses gently applied around the eye area**
- » Wearers of soft contact lenses (Grey glasses)
- » A single pass with a sterile cotton bud rolled across the ulcer will deplete the viral load.

1. **Acyclovir 3% eye ointment** (Lovir, Santovir, Zovirax)
Insert 1cm ointment into lower conjunctival sac 5 times daily at 4 every 2 hourly for minimum 3 days.
2. **Prevention of secondary bacterial infection if present**
 - » **Moxifloxacin 0.5% eye drops** (Moxiral, Moxigan, Megamox) x 1 drop in affected eye for 2-3 days if not improved than 5 days

Immunodeficient patients or patients who respond poorly to topical therapy or frequent recurrences or severe B/L disease

» **Tab. Acyclovir 400mg** (Acylex, Aclovir)
1-0-1 OR 1-1-1 (BD/TDS)

Topical steroids: These are avoided unless significant disciform keratitis is also present. Steroid eye drops are contraindicated except under the strict supervision of an ophthalmologist.



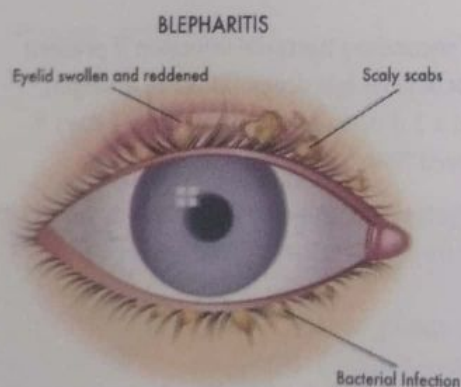
BLEPHARITIS (BLEPHARITIS SQUAMOSA)

- » **Definition:** Blepharitis is a common eyelid condition that presents as a chronic and/or recurrent inflammation with scaling of the eyelid margins.
- » **Cause:** The common cause of prolonged red eye due to inflammation of the eyelash follicles along the edge of the eyelid. The most common cause is overgrowth of *S. epidermidis* (Staphylococci), and the inflammation is largely a reaction to the delta like toxin produced by the bacteria.
- » The disorder is associated with seborrheic dermatitis, atopic dermatitis, and occasionally eyelash infestation with lice or infection with *S. aureus*.
- » **Classification**
 - » **Anterior blepharitis:** inflammation of the anterior margin of the eyelids, involving the skin, eyelashes, and follicles
 - » **Posterior blepharitis:** inflammation of the posterior margin of the eyelids; associated with meibomian gland dysfunction and/or obstruction (meibomitis) as well as abnormalities of the tarsal plate

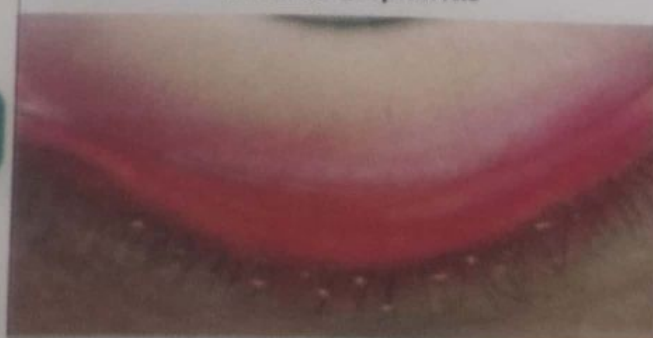
△ Blepharitis

C/C:

- » Chronic or recurrent red, swollen eyelids and irregular eyelid margins
- » Crusty, scaly plaques, and/or oily deposits on the eyelid margin and eyelashes
- » **Eye irritation and visual abnormalities**
 - ↳ Eye Pain, Itchiness
 - ↳ Foreign body sensation
 - ↳ watering of the eye
 - ↳ Photophobia
 - ↳ Blurred vision.



Anterior blepharitis



Rx Treatment for Children's

1. **Eyelid margin hygiene** - Careful daily cleansing of the edges of the eyelids and eyelashes.
2. **Syp. Azithromycin 200mg/5ml** (Azomax, Zetro) x OD
3. **Sulfacetamide Sodium 100mg + Prednisolone Acetate 2mg eye drops** (Blephamide, Mydosone, Blephapred) 1 drops 4 times a day for 1 month
4. **Sulfacetamide Sodium 100mg + Prednisolone Acetate 2mg eye ointment** (Blephamide, Mydosone, Blephapred) x Apply at night only for 1 month
5. **Artificial tear eye drops** (Tear plus, Optitears, Visol gel)

Rx

Treatment for Adults

1. **Eyelid margin hygiene** - Careful daily cleansing of the edges of the eyelids and eyelashes.
2. **Tab. Azithromycin 500mg** (Azomax, Zetro) x OD
3. **Sulfacetamide Sodium 100mg + Prednisolone Acetate 2mg eye drops** (Blephamide, Mydosone, Blephapred) 1 drops 4 times a day for 1 month
4. **Sulfacetamide Sodium 100mg + Prednisolone Acetate 2mg eye ointment** (Blephamide, Mydosone, Blephapred) x Apply at night only for 1 month
5. **Artificial tear eye drops** (Tear plus, Optitears, Visol gel)

Posterior blepharitis



CORNEAL ABRASION

Definition: scrape or scratch injury (mechanical or chemical disruption) on the corneal epithelium.

Epidemiology: Most common eye injury among children's, and probably in general population.

Lesion heal very quickly (24-48); time to healing depends on how deeply the cornea was involve.

Typical causes:

- » **Direct injury:** finger nails, mascara brushes, branches, chemical injuries (i.e. mace)
- » Foreign matter stuck under the eyelid, Blowing dust or debris
- » Prolonged contact lens wear or improperly fitted lenses
- » **Other causes:** iatrogenic (during procedure), Entropion, UV light (i.e., UV keratitis), Thermal burns (e.g., cigarettes, matches), Trachoma and Dry eyes (e.g., Sjogren syndrome)

△ Corneal abrasion

- C/C:**
- » Foreign body sensation in the eye
 - » Eye pain
 - » Epiphora
 - » Blurred vision
 - » Photophobia
 - » Conjunctival injection

Diagnosis:

- » **History:** injury
- » **Sensation:** Pain, Photophobia
- » **Vision:** Decreased if central
- » **Discharge:** tearing
- » **Pupillary Right Reflex (PLR):** Brisk
- » **Conjunctival injection:** Diffuse
- » **Corneal appearance:** stains with fluorescein
- » **Intraocular Pressure (IOP):** Normal

Rx

Treatment of corneal abrasion

- » Removal of any retained foreign object.
 - » **If pain Analgesia:** oral NSAIDs, topical NSAIDs (Diclofenac, ketorolac), or narcotics, depending on pain severity.
 - » **Infection prophylaxis** → antibiotic eye drops.
1. **Ciprofloxacin 0.3% eye drops** (Ciloxan, Ethiflox, Rocip)
 - 1 drops in affected eye 4-5 times a day.
 - OR **Moxifloxacin 0.5% eye drops** (Moxiral, Moxigan, Megamox)
 - 1 drop 3 times a day in affected eye for 5-7 days

2. Oral/topical analgesia If eye pain:

- » **Ketorolac 0.5% eye drops** (Ketrosan, Ketrol)
- » **Tab. Diclofenac sodium 50mg** (Voren, Voltal) x BD/TDS



SUBCONJUNCTIVAL HEMORRHAGE

Definition: injury to the eye leading to hemorrhage beneath the conjunctiva

△ Subconjunctival Hemorrhage

C/C:

Diagnosis:

- » **History:** trauma, hypertension, incidental, diabetes, coagulopathy
- » **Sensation:** none, mild irritation
- » **Vision:** Normal
- » **Discharge:** None
- » **Pupillary Right Reflex (PLR):** Brisk
- » **Conjunctival injection:** localised, bright red
- » **Corneal appearance:** clear
- » **Intraocular Pressure (IOP):** Normal

Rx

- » Reassurance – it's a benign and self-limiting condition.
- » **Prognosis:** clears within 1-2 weeks.
- » **If recurrent**
 - » Coagulation profile
 - » Bed side sugar level, HBA1C
 - » Check blood pressure, if high Rx accordingly
- » **Otherwise no treatment required**



OCULAR CHEMICAL BURNS INJURIES (NON-MECHANICAL)

Acid burns

- » Acid burns are less serious than alkali burns.
- » Common acids responsible for burns are: sulphuric acid, hydrochloric acid and nitric acid.

Alkali burns

- » Alkali burns are among the most severe chemical injuries known to the ophthalmologists.
- » Common alkalies responsible: lime, caustic potash or caustic soda and liquid ammonia (most harmful).

△ Ocular Chemical Burns C/C:

- » Conjunctival injection
- » Intense pain
- » Visual impairment
- » **Blepharospasm**: involuntary eyelid closure
- » Erythematous conjunctiva or whitening of the conjunctiva
- » Photophobia

Diagnosis:

- » **History**: chemicals incidentally or chemical attacks.
- » **Sensation**: intense pain, photophobia
- » **Vision**: mildly decreased
- » **Pupillary Right Reflex (PLR)**:
- » **Conjunctival injection**: +ve
- » **Corneal appearance**: see classification
- » **Intraocular Pressure (IOP)**:
- » **pH**: ↑↑ (Normal pH)

Grades of chemical burns (Roper-Hall classification)

Grade-I: Clear cornea, no conjunctival or limb ischemia & Visual prognosis excellent.

Grade-II: Cornea hazy but iris detail visible, conjunctival ischemia: <1/3, & Visual prognosis are good

Grade-III: Opaque cornea, total epithelial loss, iris detail obscured, conjunctival ischemia 1/3 to 1/2, Visual Prognosis: doubtful/guarded

Grade-IV

Cornea opaque, no view of the iris and pupil, conjunctival ischemia >1/2, Visual prognosis: poor

Rx

- » **Note**. Do not waste time on history and examination of the patient; it should be done after the irrigation.
- » **Oncall consultation**: Patients should be advised to irrigate with a copious volume of water or saline for at least 15 minutes before arrival to the ED because immediate irrigation is the most important factor in preventing morbidity.
- » **Prevent further damage by following measures**:
 - » Immediate and thorough irrigation with the available cold tap **clean water** or **normal saline** delivered through an IV tubing. Deliver minimum of 2L of water in 20-30 minutes or until the pH normalizes/restored for acidic agents.
- » **Mechanical removal of contaminant**. If any particles are left behind, particularly in the case of lime, these should be removed carefully with a swab stick.
 - » Removal of contaminated and necrotic tissue
 - » Necrosed conjunctiva should be excised.
 - » Contaminated and necrosed corneal epithelium should be removed with a cotton swab stick.
 - » **Ophthalmologic consultation**.
- » **Maintenance of favorable conditions for rapid & uncomplicated healing by following measures**:
 - » **Antibiotic Eye Drops**: Moxifloxacin, Ciprofloxacin
 - » **Steroid Eye Drops after Ophth. Consultation**: to reduce inflammation, neutrophil infiltration, & address Ant. Uveitis. **Cautious** use is recommended **after 2 weeks**, as steroids may interfere with collagen synthesis.
 - » **Sodium citrate**: used as 10% topical eye drops stabilizes neutrophils and reduces collagenase release.
 - » **Cycloplegic**: Atropine, may improve the comfort.
 - » **Lubricant eye drops** (Preservative free) should be used in abundance to promote the healing.
 - » Treatment of complication according to hospital guidelines

Topical antibiotics

- » **Moxifloxacin 0.5% eye drops** (Moxiral, Moxigan, Megamox)
1 drop 4-5 times in affected eye to prevent infection

In severe cases, antibiotic ointment at night may be required.

- » **Polyfax eye ointment** apply at night



CORNEAL FOREIGN BODIES (MECHANICAL)

- Corneal foreign bodies are usually superficial and benign, but penetration of a foreign body into the globe can cause loss of vision. Foreign bodies are generally small pieces of metal, wood, or plastic that become embedded in the cornea. The presence of a corneal foreign body causes an inflammatory reaction, dilating blood vessels of the conjunctiva and causing edema of the lids, conjunctiva, and cornea.
- Ask about details surrounding the onset of symptoms, including patient activity. If a cause is not obvious, ask about all activities in the previous 24 hours, especially activities that cause high-velocity projectiles. High velocity globe penetration injuries include grinding, hammering metal on metal, or operation of other high-speed machinery.
- Visual acuity should be normal. Inspection of the eye may reveal edema of the eyelid and diffuse or focal/perilimbal conjunctival injection.
- Occasionally, the foreign body may be visible with the naked eye. Evert the lid to identify and remove other foreign bodies that may be present. When a metallic foreign body is present for more than a few hours, a rust ring develops around the metal.
- Foreign bodies present for >24 hours may be surrounded by a white ring representing a WBC infiltrate. Anterior chamber flare and cells and a corneal foreign body are identifiable on slit lamp examination
- The presence of a gross hyphema or a microhyphema evident in the anterior chamber on slit lamp examination suggests globe perforation.
- If the foreign body has penetrated the cornea, the tract of the projectile may be seen. The Seidel test may be positive with penetration of the globe

△ Corneal Foreign body C/C:

- The patient will usually complain of a "foreign body" sensation during blinking.
- Tearing
- Blurred vision
- Photophobia

Prophylaxis

- Industrial and agricultural workers should be advised to use special protective glasses.
- Cyclists and scooterists should be advised to use protective plain glasses or tinted goggles.
- Special guards should be put on grinding machines and use of tools with overhanging margins should be banned.
- Eye health care education should be imparted, especially to the industrial and agricultural workers.



Corneal Foreign Body Removal

- Corneal foreign bodies should be removed carefully, with the patient and physician seated at each other's eye level, and under the best magnification available.
- Anesthetize the cornea with a local anesthetic: Eye is anaesthetized with topical instillation of 2 to 4% Xylocaine/0.5% proparacaine and the patient is made to lie supine on an examination table.
- Anesthetizing both eyes is helpful, because that can eliminate reflex blinking during attempts at foreign body removal.
- Lids are separated with universal eye speculum, the patient is asked to look straight upward and light is focused on the cornea.
- Initially irrigate with normal saline, as a very superficial foreign body may be irrigated off the cornea. Next an attempt is made to remove the foreign body with the help of a wet cotton swap stick (dislodge the foreign body with a moistened cotton applicator). If it fails then foreign body spud or hypodermic needle is used.
- Efforts at removal may themselves cause corneal abrasion.
- Extra care is taken while removing a deep corneal foreign body, as it may enter the anterior chamber during manoeuvring.
- If such a foreign body happens to be magnetic, it is removed with a hand-held magnet.
- If the foreign body is tightly adherent to or embedded in the cornea, inspect the cornea using the slit lamp to assess the depth of penetration
- Full-thickness corneal foreign bodies should be removed by an ophthalmologist.
- After removal of foreign body, patching with antibiotic eye ointment is applied for 24 to 48 hours. Antibiotic eye drops are instilled 3-4 times a day for about a week.



ACUTE ANGLE CLOSURE GLAUCOMA (AACG)

- Angle-Closure Glaucoma (also called Closed-Angle Glaucoma): an attack of sudden and sharp increase in intraocular pressure caused by an obstruction of aqueous outflow (most commonly as a result of an occlusion of the iridocorneal angle) and associated with optic neuropathy and visual field defects
- Acute Angle-Closure Glaucoma (AACG): sudden obstruction of the iridocorneal angle causing a rapid, acutely symptomatic, and vision-threatening elevation of IOP, often > 30 mm Hg.
- It usually does not terminate of its own and thus if not treated lasts for many days.
- It is a sight-threatening emergency, as it can cause permanent vision loss if left untreated!

Clinical features

- Sudden onset of symptoms
- Pain:** Unilaterally inflamed, reddened, and sudden onset of severely painful eye (hard on palpation), which radiates along the branches of 5th cranial nerve.
- Rapidly progressive impairment of vision, photophobia and lacrimation developed in all cases
- Frontal headache, Nausea and vomiting.
- Blurred vision and color halos seen around light
- Cloudy cornea (opacification).
- Mid-dilated, irregular, unresponsive pupil.

Complications: rapid permanent vision loss due to ischemia and atrophy of the optic nerve

Past history: About 5% patients give history of typical previous intermittent attacks of subacute angle-closure.

Diagnostic investigation

- Tests to assess for glaucomatous damage should be performed in all patients.
 - Optic disc changes (slit-lamp examination or undilated fundoscopy)
 - Visual acuity
 - Visual field testing
- Tonometry:** all patients with suspected cases
- Gonioscopy**
- Slit-lamp examination**
- Direct fundoscopy (with undilated pupils)** - an alternative to slit-lamp examination to assess for optic disc damage.

Diagnosis:

- History:** change of lighting, worse in dim light
- Sensation:** pain, photophobia
- Vision:** decreased
- Discharge:** tearing
- Pupillary Right Reflex (PLR):** mild dilated and fixed. (OR semidilated, vertically oval and fixed)
- Conjunctival injection:** diffuse
- Corneal appearance:** cloudy cornea
- Intraocular Pressure (IOP):** markedly elevated (> 30 mm Hg) on tonometry.
- Gonioscopy:** Narrowing/closure of the iridocorneal angle (e.g. iridotrabecular contact)
- Slit-lamp examination:** very shallow, aqueous flare or cells may be seen in anterior chamber.



As GP - Urgent ophthalmic referral

- AACG is a serious emergency and should be initially managed with IOP-decreasing medications that have a rapid onset of action. Once IOP has decreased, patients should undergo a definitive procedure as soon as possible to prevent recurrence.
- Steps to managed AACG aggressively as below:**
 - General considerations
 - Immediate medical therapy to lower IOP
 - Definitive treatment
 - Prophylaxis of the fellow eye
 - Long-term glaucoma surveillance and IOP management of both eyes.
- General considerations**
 - Emergency ophthalmology consultation
 - Place the patient in a supine position.
 - Ensure the contralateral eye has been evaluated for urgent treatment, even if it is asymptomatic.
 - Administer supportive care as needed.
 - Analgesia for Pain management:** IV Ketorolac 30mg/1ml (Toradol, Ketor)
 - Antiemetics:** IV Ondansetron 8mg/2ml (Onset)



Immediate medical therapy to lower IOP: There is currently no standardized recommendation for empiric management of AACG. The following regimen may be followed with due consideration of any comorbidities.

- » **Topical eye drops:** Administer the following eye drops in succession, one minute apart:
 - **Direct parasympathomimetic:** Topical Pilocarpine becomes effective only once IOP decreases to < 40 mm Hg.
 - **Alpha-2 agonist:** Brimonidine
 - **Beta blocker:** Timolol 0.25% or 0.5%
- » **PLUS Systemic carbonic anhydrase inhibitor:** Acetazolamide 500mg (AZM) stat followed by 250 mg tablet 2 or 3 times a day.
- » **Consider also the following alternatives:**
 - Betaxolol 0.25% eye drops: Betoptic-S
 - Brinzolamide 0.1% eye drops: Azopt
 - Dorzolamide 2% + Timolol 0.5% eye drops: Combigen, Cosopt, Glantrim
 - Levobunolol 0.5% eye drops: Betagan, Betabar, Levosan
 - Brimonidine 0.2% eye drops: Alphagan

If IOP is still elevated after 30–60 minutes:

The following should be given only under the guidance of an ophthalmologist.

- » Repeat eye drops from above up to three times.
- » Consider a systemic hyperosmotic agent if IOP remains high after 60 minutes of initiating therapy.
 - **In patients with nausea:** IV mannitol 250–300ml according body weight x IV state
 - **In patients without significant nausea**
 - **Nondiabetic patients:** oral glycerine
 - **Diabetic patients:** oral isosorbide

If IOP is decreasing: Examine for other signs of resolution of the acute attack.

- » Symptomatic improvement (decreased pain and nausea; improvement of vision)
- » Clear cornea (resolution of corneal edema)
- » Decreased conjunctival hyperemia
- » Normal pupillary size and reaction

Note: Do not use mydriatic drugs (e.g., atropine and epinephrine) during ophthalmologic examination in patients with acute angle-closure glaucoma! Moreover, do not cover the eye, since darkness induces mydriasis and worsens the condition!

Urgent interventional therapy

- » **Anterior chamber paracentesis**
 - » **Indication:** Consider for vision-threatening elevation in IOP refractory to medical management.
 - » **Procedure:** controlled drainage of some of the aqueous humor through an opening created at the limbus
 - » **Important consideration:** Anterior chamber paracentesis is a temporizing measure; patients will still require definitive treatment with laser peripheral iridotomy.
- » **Definitive treatment**
 1. **Urgent laser peripheral iridotomy**
 - **Indication:** all patients within 24–48 hours of resolution of the acute attack
 - **Laser peripheral iridotomy (LPI):** Gonioscopy should be performed as soon as cornea becomes clear. Laser PI should be performed if PAS are seen in $< 270^\circ$ angle. LPI re-establishes communication between posterior and anterior chamber, so it by passes the pupillary block and immediately relieves the crowding of the angle.
 - **Laser peripheral iridotomy (with Nd:YAG laser or Argon Laser)** should always be preferred over surgical PI. However, if lasers are not available surgical PI should be done (See page 260 for technique).
 2. **Filtration surgery:** i.e. trabeculectomy should be performed in cases where IOP is not controlled with the maximum medical therapy following an attack of acute PAC or when gonioscopy reveals PAS $> 270^\circ$ angle and also when peripheral iridotomy is not effective.
 3. **Clear lens extraction** by phacoemulsification with intraocular lens implantation has recently been recommended by some workers, especially in the presence of phacomorphic etiology (Dx on UBM).
- » **Prophylactic treatment in the normal fellow eye** - Prophylactic laser iridotomy (preferably) or surgical peripheral iridectomy should be performed on the fellow asymptomatic eye (PACS) as early as possible as chances of acute attack are 50% in such eyes.
- » **Long-term glaucoma surveillance and IOP management in both eyes** of a patient with acute Primary Angle Closure Glaucoma is must to ultimately prevent glaucomatous blindness:
 - Eyes treated with PI (both affected and fellow eye) may develop PACG at any time. So, it should be treated as and when required.
 - Filtration surgery may fail anytime during the course and hence need to be repeated with antimetabolites.



EYE/OPHTHALMIC DRUG BRANDS IN PAKISTAN

Fluorometholone	» FML Eye drops » Florozil Eye drops » Flucon Eye drops
Fluorometholone + Tetrahydrozoline	» Femicon Eye Drops
Fluorometholone + Neomycin	» Eyfem-N Eye Drops
Dexamethasone	» Maxidex eye drops
Dexamethasone + Neomycin	» Optadex Eye drops
Chloramphenicol	» Chloroptic Eye drops » Optachlor Eye drops » Optachlor Eye ointment » Santochlor 0.5% Eye drops
Dexamethasone + Chloramphenicol	» Methachlor Eye drops » Methachlor Eye ointment » Tobra-D Eye drops » Vegadex-C Eye drops » Dexachlor Eye drops » Medidex-C Eye drops » Eyebradex Eye drops
Chloramphenicol + Dexamethasone + Tetrahydrozoline	» Spersadexoline Eye drops
Polymyxin-B + Neomycin Sulphate + Dexamethasone	» Maxitrol Eye Drops » Maxitrol Eye Ointments
Betamethasone Sodium Phosphate	» Betnesol-N Eye Ointment
Prednisolone Acetate	» Pred Forte Eye drops » Fortipred Eye Drops » Mildopred Eye Drops
Prednisolone + Chloramphenicol	» Prednisynth Eye drops » Prednicol Eye drops
Naphazoline	» Curine Eye Drops » Naphcon Forte Eye Drops
Naphazoline + Pheniramine Maleate	» Naphcon-A Eye Drop » Ocucon-A Eye Drops
Antazoline + Naphazoline	» Curall-A Eye Drops
Sulfacetamide Sodium + Prednisolone Acetate	» Blephamide Eye drops
polymyxin B + bacitracin	» Polyfax Eye Ointment
Tobramycin	» Nebra Eye drops » Nebra Eye Ointments » Tobrex Eye drops
Tobramycin + Dexamethasone	» Tobrex Eye Ointments » Tobradex Eye drops » Tobradex Eye ointments » Veflox-D Eye drops



Ofloxacin	» Amygdex Eye drops » Exocin Eye drops » Oflocin Eye drops » Optoflox Eye drops » Oflexer Eye drops » Tariflox Eye drops
Ofloxacin + Dexamethasone	» Oflocin-D Eye drops » Dexoflox Eye drops
Ciprofloxacin	» Ciloxan Eye drops » Quinoflox Eye drops » Rocip Eye drops
Levofloxacin	» Lequix Eye drops » Qumic Eye drops » Xeflox Eye drops
Moxifloxacin	» Vigamox Eye Drops » Moxigan Eye drops » Ocumox Eye Drops » Ocumox eye ointment » X-gen Eye drops » Oxcin Eye drops
Moxifloxacin + Dexamethasone	» Oxcin-D eye drops
Hydroxypropyl Methylcellulose	» Hicel Eye drops
Polyvilyl alcohol	» Tear plus Eye drops
Polyethylene Glycol, Propylene Glycol	» Systane Eye Drops » Eyelub Eye drops » Eyecane Eye drops
Polyacrylic acid	» Polytek Eye drops » Visogel Eye drops » Acrogel
Polymyxin B, Neomycin, Bacitracin, Hydrocortisone	» Cortisporin Eye Ointment
Oxytetracycline + Polymyxin B	» Xinox Eye Ointment
Polymyxin B and Zinc Bacitracin	» Trimin Eye Ointment
Tobramycin + Loteprednol etabonate	» Nebralot Eye drops
Sodium Cromoglycate + Tetrahydrozoline	» Histazolin Eye drops
Phenylephrine HCL + Pyrilmamine Maleate + Antipyrine	» Preffrin-A Eye drops
Phenylephrine (HCl) + Pyrilmamine (Maleate)	» Decon-A Eye Drops
Olapatadine	» Xepat 0.1% Eye drops » Xepat forte (0.2%) Eye drops » Patadin Eye drops
Lodoxamide Tromethamine	» Alomide Eye Drops
Cyclopentolate	» Nafamine Eye Drops
Chlorobutanol	» Lacri-lube Eye Ointment
Tropicamide	» Mydrasyl Eye drops » Ophth-Dilate Eye drops
Timolol	» Blotim 0.25% Eye Drops » Blotim 0.5% Eye Drops



Betaxolol	» Betoptic 0.25% & 0.5% Eye drops
Brinzolamide/Brimonidine	» Simbrinza Eye drops
Brimonidine + Timolol	» Brimo-T Eye drops
Brinzolamide	» Azopt Eye Drops
Brimonidine tartrate	» Alphagan Eye Drops
Latanoprost	» Xalatan Eye Drops
	» Prostilet Eye Drops
	» Latep Eye Drops
Travoprost	» Travatan Eye drops
	» Travost Eye Drops
Bimatoprost	» Lumigan Eye Drops
Proparacaine	» Alcaine Eye drops
Dorzolamide + Timolol	» SyniGan Eye drops
	» Glantrim Eye Drops
	» Tilomide Eye drops
Nepafenac	» Nevanac Eye drops
	» Avanep Eye drops
	» Ilevro
	» Acukast Eye drops
	» Barinep Eye drops
Diclofenac sodium	» Oclonac Eye drops
	» Konac Eye drops
	» Diclomin Eye drops
Flurbiprofen	» Ocufen Eye Drops
	» Optofen Eye drops
Ketorolac	» Ketrosan Eye drops
Ketotifen	» Ketot Eye drops
	» Ketrol Eye drops
Atropine	» Ophth-atropine Eye drops
	» Azopt Eye drops
Vitamin-A Palmitate	» Ophth-Vit-A Eye drops
Tetracycline	» Ophth-tetracyl Eye Ointment





ACUTE TONSILLITIS & PHARYNGITIS

Clinical features

- » Acute bacterial tonsillo-pharyngitis
 - » Sudden onset of symptoms: fever, sore throat, dysphagia
 - » Significantly inflamed pharynx
 - » Pharyngeal and/or tonsillar erythema and edema
 - » Pharyngeal and/or tonsillar exudates (rare in children < 3 years of age)
 - » Palatal petechiae
 - » Cervical lymphadenitis: Tender, enlarged cervical lymph nodes (Bilateral jugulodigastric lymph nodes).
 - » Absence of cough
 - » Acute GAS tonsillopharyngitis can also present as scarlet fever with: strawberry tongue, scarlatiniform rash.
- » Acute viral tonsillopharyngitis: Cough, Coryza (common cold), Rhinorrhea (Runny nose), Oral ulcers/stomatitis, Conjunctivitis, Diarrhea and Absence of fever
- » **Red flags for tonsillopharyngitis:** Trismus, Drooling, Asymmetric tonsils, displaced uvula, unilateral facial swelling, Muffled or "hot potato" voice, Clinical features of sepsis and immunosuppression.
- » The presence of any of the **red flag features** may indicate suppurative and/or invasive complications of acute tonsillitis and/or pharyngitis, such as deep neck infections (e.g., peritonsillar abscess, retropharyngeal abscess), cervical lymphadenitis, mastoiditis, and rarely, sepsis.
- » If red flags for tonsillopharyngitis are present:
 - » Refer or consult ENT urgently.
 - » Identify and treat deep neck infections.
 - » Consider empiric IV antibiotics and steroids for patients with signs of airway compromise, and prepare for difficult airway management as needed.

Diagnostic workup

- » Clinical evaluation:
 1. Patient History:
 - » Onset, duration, and severity of symptoms
 - » Previous episodes of tonsillitis or pharyngitis
 - » Recent exposure to individuals with similar symptoms
 - » Presence of known risk factors (e.g., smoking, allergies, recent upper respiratory infections)
 2. Physical Examination:
 1. Throat Inspection:
 - » Redness and swelling of the tonsils and pharynx
 - » Presence of white or yellow exudates or patches on the tonsils
 - » Enlargement of the tonsils (hypertrophy)
 2. Palpation: Tender and swollen cervical lymph nodes
 3. Vital Signs: Fever (temperature above 38°C or 100.4°F)
- » Diagnostic Tests
 1. Rapid Antigen Detection Test (RADT):
 - » Quick test for detecting Group A Streptococcus (GAS) bacteria
 - » High specificity but varying sensitivity
 2. Throat Culture:
 - » Swab of the throat and tonsils sent to a lab to identify the presence of bacteria
 - » Considered the gold standard for diagnosing streptococcal pharyngitis
 - » Results take 24-48 hours
 3. Blood Tests:
 - » Complete Blood Count (CBC): To check for elevated white blood cells (indicative of infection)
 - » Inflammatory markers: serum ESR, CRP
 - » Monospot Test: For infectious mononucleosis (if Epstein-Barr virus is suspected)
 - » Antistreptolysin O (ASO) Titer: To detect a recent streptococcal infection



CLINICAL SCORING – MODIFIED CENTOR SCORE

Criterion		points
Age	3–14 years	+1
	15–44 years	0
	> 44 years	-1
Exudate or swelling on tonsils	Yes	+1
	No	0
Tender or swollen anterior cervical lymph nodes	Yes	+1
	No	0
Temperature > 100.4°F (38°C)	Yes	+1
	No	0
Cough	Absent	+1
	Present	0
Interpretation Score ≤ 1: no further diagnostic testing needed Score ≥ 2: Consider rapid strep test and/or throat culture. Score ≥ 4: Consider empiric antibiotic therapy (controversial)		

Rx

General and supportive measures

- » Bed rest, plenty of fluids
- » Consider household remedies such as warm-saline (salt water) gargles or pharyngeal irrigations or medicated gargle (Benzarin, Listerine) x 2-3 time daily
- » Consider oral topical local anesthetics for throat discomfort in severe cases: e.g., benzocaine lozenges, phenol throat sprays, compounded mouthwash.

Guidelines:

- » GAS pharyngitis and/or tonsillitis: typically self-limited; prescribe antibiotics to prevent complications (e.g., peritonsillar abscess, rheumatic fever) and decrease transmission.
- » Acute viral tonsillopharyngitis: self-limited; continue supportive care and provide patient education. Improvement can be expected within 3–4 days.

Antibiotic therapy for 7-10 days: Indicated for patients with laboratory confirmation of GAS infection

- ↳ Tab. Co-Amoxiclav 625mg (Augmentin, Calamox) x TDS for 10 days
- ↳ OR Tab. Azithromycin 500mg (Azomax, Azitma) x OD for 5 days
- ↳ OR Tab. Clarithromycin XL 500mg (Claritek XL, Klaricid XL) x OD for 10 days
- ↳ OR Cap. Cephalexin 500mg (Ceporex, Keflex) x BD for 10 days
- ↳ OR Cap. Cefadroxil 500mg (Cedrox, Duricef) x BD for 10 days

Analgesia/antipyretics:

- » Tab. Ibuprofen 400mg (Brufen) x three times a day
- OR Tab. Paracetamol 500mg (Panadol, Calpol) at dose 500mg – 1000mg (1-2 tablets) x three times a day

2nd Generation Antihistamine: If patients present with sneezing, coryza, itchy throat

- ↳ OR Tab. Loratidine 10mg (Softin, Loril, Lorin-NSA)
- ↳ OR Tab. Desloratidine 5mg (Desora, Jordin-D) x OD
- ↳ OR Tab. Fexofenadine 180mg (Telfast, Fexo) x OD
- ↳ OR Tab. Levocetirizine 5mg (Belair, T-day) x OD
- 0 – 0 – 1 (Orally once daily (OD) when required)

If symptoms of allergy, hay fever, cough and common cold,

- ↳ Syp. Corex-D OR Syp. Hydrillin OR Syp. Cofrest
- 1-2 teaspoonful TDS



ACUTE SINUSITIS (ACUTE RHINO-SINUSITIS)

- Definition:** Acute sinusitis (also commonly known as acute rhinosinusitis) is a symptomatic inflammation of the mucosal lining of the nasal cavity and paranasal sinuses, presenting with purulent nasal drainage accompanied by nasal obstruction, facial pain/pressure/fullness, or both for 4 weeks or less.
- Etiology:** viral infection (most common), will progress to acute bacterial sinusitis → *Strept pneumoniae* (35%), *Haemophilus influenzae* (40%), *Moraxella catarrhalis* (20%), and beta-hemolytic streptococci *S. pyogenes* (8%)
- Route of transmission:** droplet transmission, particularly in winter months
- Risk factors:**
- » **Preexisting viral URTI:** most common; leads to superimposed bacterial infections
 - » **Ventilation disorders of the sinuses:** Hypertrophy of nasal turbinates, nasal polyps, deviation of nasal septum, ciliary dysfunction (such as cystic fibrosis, primary ciliary dyskinesia), *Concha bullosa*
 - » Foreign body lodged in the nasal cavity, odontogenic infection (leads to unilateral maxillary sinusitis), allergic rhinitis (spread of pathogens via nasal mucosa), bronchial asthma, aspirin sensitivity

Clinical features

- » Alteration in the sense of smell, hyposmia or Anosmia (Loss of smell)
- » Blockage (nasal obstruction)
- » Congestion/ Cough
- » Discharge: Purulent nasal discharge, anterior, or posterior in the form of postnasal drip.
- » Ear pressure/fullness
- » Facial pain/pressure/tenderness, Fever
- » Fatigue/Generalized malaise
- » Headache/Halitosis

Clinical classification as:

- » **Acute sinusitis:** symptoms for ≤ 4 weeks with complete resolution.
- » **Subacute sinusitis:** symptoms for 4-12 weeks
- » **Chronic sinusitis:** symptoms for ≥ 12 weeks (12 or more episode/weeks)
- » **Recurrent acute sinusitis:** symptoms for 4 or more episodes of sinusitis per year, lasting for more than 7-10 days.

Severity: Characterized according to the presence of fever with purulent nasal discharge, moderate to severe facial or dental pain, or periorbital swelling lasting for at least 3-4 days.

Diagnostic workup

- » **Clinical diagnosis:** Based on history and physical exam.
- » **Investigations:** Usually no need for further investigations unless there are complications.
 - » **X-Ray PNS:** initial but not appropriate, may show air-fluid level of the involved sinuses.
 - » **CT maxillofacial or PNS** (with or without contrast) – investigation of choice.

Note: Observe patient for up to 7 days before giving antibiotics, if symptoms worsen or do not improve during observation → Treat with antibiotics for 5 – 10 days.



TREATMENT OF ACUTE VIRAL SINUSITIS

Supportive treatment

- » Usually self-limiting – patients improves within 7 – 10 days
- » Adequate rest, hydration & warm facial packs may be useful
- » **Advice nasal saline irrigations/sprays for symptomatic relief:** useful for treating congestion by reducing inflammation, thin the mucus, wash out bacteria and have the add advantage to decreasing medication use → **Norsaline-P drops** x 2-3 sprays/drops into each nostril every 2-4 hours.
- » **Steam inhalation:** Steam alone or medicated with **Vicks** or **Tincture Benzoin Co.** or menthol provides symptomatic relief and encourages sinus drainage. Inhalation should be given 15 – 20 min after nasal decongestion for better penetration.
- » **Topical nasal decongestant** (oxymetazoline spray) are often preferred over oral pseudoephedrine because of increased potency and less risk of adverse effects.
 - » **Topical oxymetazoline spray** (xynoline or xolisan nasal spray) x 2-3 sprays in each nostril twice daily for 3-5 days, to prevent the occurrence of rebound congestion.
- » **Analgesia/antipyretics:**
 - » **Tab. Ibuprofen 400mg** (Brufen) x three times a day OR **Tab. Paracetamol 500mg** (Panadol, Calpol) at dose 500mg – 1000mg (1-2 tablets) x three times a day
- » **Intranasal steroids:** May decrease allergic response in patients with allergic rhinitis & therefore decrease edema, swelling associated with sinusitis. Treatment for at least 1 month is recommended, depends on course of disease.
 - » **Mometasone nasal spray** (Rinelon or Hivate nasal spray) x 2-3 sprays in each nostril twice daily.



TREATMENT OF ACUTE BACTERIAL SINUSITIS

1. Treatment are the same as acute viral sinusitis see above
2. **Tab. Co-Amoxiclavate 625mg** (Augmentin, Calamox) x TDS OR **Cap. Doxycycline 100mg** (Doxyn, Vibramycin) x BD OR **Tab. Levofloxacin 500mg** (Cravit, Levoxin, Leflox) x OD OR **Tab. Moxifloxacin 500mg** (Xefecta, Avelox, Maxlox) x OD



CHRONIC SINUSITIS (CHRONIC RHINO-SINUSITIS)

- Definition: When symptoms of sinusitis persist for more than 3 months (> 12 weeks) chronic state develops.
- Most important cause of chronic sinusitis is failure of acute infection to resolve.
- Risk factors: Hypertrophy of nasal turbinates, nasal polyps, deviation of nasal septum, Ciliary dysfunction (such as cystic fibrosis, primary ciliary dyskinesia), Concha bullosa deformity, Foreign body lodged in the nasal cavity, odontogenic infection (leads to unilateral maxillary sinusitis), allergic rhinitis (spread of pathogens via nasal mucosa), history of bronchial asthma, aspirins sensitivity, chronic granulomatosis with polyangiitis, sarcoidosis

DIAGNOSTIC CRITERIA FOR CHRONIC RHINO-SINUSITIS (American Academy of Otolaryngology)

- Twelve weeks or longer of two or more of the following signs and symptoms:
- » Mucopurulent drainage (anterior, posterior, or both)
 - » Nasal obstruction (congestion)
 - » Facial pain/pressure/fullness
 - » Decreased sense of smell.
- Inflammation is documented by one or more of the following findings:
- » Purulent (not clear) mucus or edema in the middle meatus or anterior ethmoid region
 - » Polyps in nasal cavity or the middle meatus, and/or
 - » Radiographic imaging showing inflammation of the paranasal sinuses.

Clinical features

Clinical presentation are often vague and similar to those of acute sinusitis but of lesser severity.

- » Alteration in the sense of smell, hyposmia or Anosmia (Loss of smell)
- » Blockage (nasal obstruction)
- » Congestion/Cough
- » Discharge: Purulent nasal discharge, anterior, or posterior in the form of postnasal drip.
- » Ear pressure/Ear fullness
- » Facial pain/pressure/tenderness, Fever
- » Fatigue/Generalized malaise
- » Headache/Halitosis

Diagnostic Workup

- » Anterior rhinoscopy: polyps, purulence from middle meatus, or structural abnormalities.
- » Nasal endoscopy may show inflammation, purulent discharge, edema, or frank polyps.
- » Investigation of choice: CT maxillofacial or PNS (with or without contrast) – opacification of involved sinuses, mucosal thickening, air-fluid levels, or anatomical abnormalities such as polyps, retention cysts, or sclerotic or thickened sinus walls
- » X-Ray PNS: Initially but not appropriate, may show air-fluid level, mucosal thickening or opacity of the involved sinuses.
- » Nasal sinus culture and sensitivity of sinus discharge helps in the proper selection of an antibiotic. Difficult to obtain, often done via anterior rhinoscopy. Endoscopically guided cultures taken directly from secretions in the middle meatus by an ENT specialist.
- » Allergy testing/RAST test: may be positive

Rx

TREATMENT OF CHRONIC RHINO-SINUSITIS

- » Advice nasal saline irrigations/sprays for symptomatic relief: Norsaline-P drops x 2-3 sprays/drops into each nostril every 2 to 4 hours.
- » Steam inhalation: Steam alone or medicated with Vicks or Tincture Benzoin Co. or Menthol provides symptomatic relief and encourages sinus drainage.
- » Intranasal steroids: Fluticasone 50mcg nasal spray (Flixonase or Ticovate) 1 sprays in each nostril twice daily OR Mometasone nasal spray (Rinelon or Hivate) x 2-3 sprays in each nostril twice daily for at least 8-12 weeks.
- » Analgesia/antipyretics:
 - ↳ Tab. Ibuprofen 400mg (Brufen) x three times a day
 - OR Tab. Paracetamol 500mg (Panadol, Calpol) at dose 500mg – 1000mg (1-2 tablets) x three times a day.
 - OR Tab. Diclofenac sodium 50mg (Voren) x BD/TDS
 - OR Tab. Aceclofenac 100mg (Acenac, Acelo) x BD
- » Antibiotic therapy for at least 10 – 14 days
 - ↳ Tab. Co-Amoxiclav 625mg (Augmentin, Calamox) x TDS
 - ↳ OR Tab. Cefuroxime axetil 250mg (Zinacef) x BD
 - ↳ OR Cap. Doxycycline 100mg (Doxyn, Vibramycin) x BD
 - ↳ OR Tab. Clarithromycin XL 500mg (Klaricid XL) x OD
 - ↳ OR Tab. Levofloxacin 500mg (Cravit, Levoxin) x OD
- » Antihistamine:
 - ↳ Tab. Fexofenadine 120mg (Fexo, Telfast) x OD
 - ↳ OR Tab. Desloratadine 5mg (Desora, Jordin-D) x OD/BD
- » Surgical indication:
 - » Evidence of structural abnormalities: e.g., polyps, masses, or anatomical obstructions
 - » Treatment failure or complications of rhinosinusitis
 - » Acute invasive fungal rhinosinusitis
- » Procedure: Functional endoscopic sinus surgery (FESS)

NON-ALLERGIC RHINITIS (NAR)

Definition: Non-allergic rhinitis (NAR) does not always involve an inflammatory process, refers to a group of chronic rhinitis subtypes that are not caused by allergy or infection, it includes infectious rhinitis, atrophic rhinitis, vasomotor rhinitis, drug-induced rhinitis, occupational rhinitis, gustatory rhinitis, hormonal rhinitis, and nonallergic rhinitis with eosinophilia syndrome (NARES). Infectious rhinitis is most often secondary to an upper respiratory tract infection that manifests as rhinosinusitis. **Vasomotor rhinitis (VMR) is most common subtype.**

Diagnostic workup

- **Clinical exam finding:** Swollen and beefy red nasal turbinates, scant mucus, cobblestoning of posterior pharynx.
- **Nasal eosinophil testing:** Once the diagnosis of NAR is established, nasal eosinophil smears are indicated
 - » Options include nasal swab or lavage or probe.
 - » Must be performed off corticosteroids, and even extensive nasal saline irrigation or swimming can cause a false-negative result.
 - » False negatives are common, but positive results are useful in identifying non-allergic rhinitis with eosinophilia syndrome.
- **Nasal endoscopy:** may be normal
- **CT maxillofacial or PNS (with or without contrast)** – Normal (not required)
- **X-Ray PNS:** Normal
- **Allergy skin prick test, allergen specific IgE test and RAST test:** Negative

Clinical features

- The presenting symptoms of NAR are indistinguishable from other forms of chronic rhinitis and include:
 - » Bilateral nasal congestion
 - » Bilateral postnasal drainage
 - » Other upper respiratory symptoms such as sneezing and rhinitis
 - » Bilateral ear fullness
 - » Symptoms on most days.
- **Key negatives in the Hx can help distinguish NAR syndromes from allergic rhinitis:**
 - » Family Hx of allergies makes NAR less likely
 - » **Symptoms do not fluctuate seasonally in NAR:** specifically, triggers are not worse outdoors during a specific pollen season in response to airborne allergens
 - » Symptoms are not exacerbated by cat or dog exposure.
- **Exacerbation of symptoms in response to** perfumes/fragrances, hairspray, potpourris, tobacco and wood smoke, changes in temperature, and barometric changes can be seen in NAR as well as in allergic rhinitis.



TREATMENT OF NON-ALLERGIC RHINITIS (NAR)

- **Avoidance of triggers:** irritants, medications, smoking
- **Nasal saline irrigations/sprays for symptomatic relief:**
 - ↳ **Norsaline-P drops** x 2-3 sprays/drops into each nostril every 2 to 4 hours.
- **Intranasal glucocorticoids and/or intranasal antihistamines**
 - » **Intranasal steroids:**
 - ↳ **Fluticasone 50mcg nasal spray** (Flixonase or Ticovate) 1-2 sprays in each nostril twice daily
 - ↳ **OR Mometasone nasal spray** (Rinelon or Hivate) x 2-3 in sprays in each nostril twice daily.
 - » **Intranasal antihistamine:**
 - ↳ **Azelastine 0.1% nasal spray** (Azosin) x 1-2 sprays in each nostril once to twice daily
 - ↳ **Olopatadine 0.6% nasal spray** (Olonase) x 2 sprays in each nostril twice daily
- **2nd Generation Antihistamine:**
 - ↳ **Tab. Cetirizine 10mg** (Zyrtec, Rigix) x OD
 - ↳ **OR Tab. Loratidine 10mg** (Softin, Loril, Lorin-NSA)
 - ↳ **OR Tab. Desloratidine 5mg** (Desora, Jordin-D) x OD
 - ↳ **OR Tab. Fexofenadine 180mg** (Telfast, Fexo) x OD
 - ↳ **OR Tab. Levocetirizine 5mg** (Belair, T-day) x OD
 - 0 – 0 – 1 {Orally once daily (OD) when required}
- **Analgesia/antipyretics:** are useful to relieve headache, fever and myalgia. Non-aspirin containing analgesics are preferable as aspirin causes increased shedding of virus.
 - ↳ **Tab. Ibuprofen 400mg** (Brufen) x three times a day
 - OR Tab. Paracetamol 500mg** (Panadol, Calpol) at dose 500mg–1000mg (1-2 tablets) x three times a day

N.B. Fexofenadine should be used with caution along with Azithromycin because combination will increase the risk of QT prolongation



CHRONIC SIMPLE RHINITIS

Name:	Age:	Sex:	Date:
Temperature:	B.P:	Pulse:	Resp. Rate:

△ Chronic simple rhinitis

C/C:

- » **Nasal obstruction:** Usually worse on lying and affects the dependent side of nose.
- » **Nasal discharge:** It may be mucoid or mucopurulent, thick and viscid and often trickles into the throat as postnasal drip.
- » Patient has a constant desire to blow the nose or clear the throat.
- » **Headache:** It is due to swollen turbinates impinging on the nasal septum.
- » **Swollen turbinates:** Nasal mucosa is dull red in colour. Turbinates are swollen; they pit on pressure and shrink with application of vasoconstrictor drops (this differentiates the condition from hypertrophic rhinitis). Middle turbinate may also be swollen and impinge on the septum.
- » **Postnasal discharge:** Mucoid or mucopurulent discharge is seen on the posterior pharyngeal wall.

Rx

1. Symptomatic treatment are same as Non-allergic R
2. Treat the cause with particular attention to sinuses, tonsils, adenoids, allergy, personal habits (smoking or alcohol indulgence), environment or work situation (smoky or dusty surroundings).
3. Nasal irrigations with alkaline solution help to keep the nose free from viscid secretions and also remove superficial infection.
4. Nasal decongestants help to relieve nasal obstruction and improve sinus ventilation. Excessive use of nasal drops and sprays should be avoided because it may lead to rhinitis medicamentosa. A short course of systemic steroids helps to wean the patients already addicted to excessive use of decongestant drops or sprays.
5. Antibiotics help to clear nasal infection and concomitant sinusitis.

HYPERTROPHIC RHINITIS (CHRONIC)

It is characterized by thickening of mucosa, submucosa, Seromucinous glands, periosteum and bone. Changes are more marked on the turbinates.

△ Hypertrophic rhinitis

C/C:

AETIOLOGY

Common causes are recurrent nasal infections, chronic sinusitis, chronic irritation of nasal mucosa due to smoking, industrial irritants, prolonged use of nasal drops and vasomotor and allergic rhinitis.

SYMPTOMS

Nasal obstruction is the predominant symptom. Nasal discharge is thick and sticky. Some complain of headache, heaviness of head or transient anosmia.

SIGNS

Examination shows hypertrophy of turbinates. Turbinal mucosa is thick and does not pit on pressure. It shows little shrinkage with vasoconstrictor drugs due to presence of underlying fibrosis.

Maximum changes are seen in the inferior turbinate. It may be hypertrophied in its entirety or only at the anterior end, posterior end or along the inferior border giving it a mulberry appearance.

Rx

- ☞ Attempt should be made to discover the cause and remove it.
- ☞ Nasal obstruction can be relieved by reduction in size of turbinates.
- ☞ **The various methods are:**
 1. Linear cauterization.
 2. Submucosal diathermy.
 3. Cryosurgery of turbinates.
 4. Partial or total turbinectomy. Hypertrophied inferior turbinate can be partially removed at its anterior end, inferior border or posterior end. Middle turbinate, if hypertrophied, can also be removed partially or totally. Excessive removal of turbinates should be avoided as it leads to persistent crusting.
 5. Submucous resection of turbinate bone. This removes bony obstruction but preserves turbinal mucosa for its function.
 6. Lasers have also been used to reduce the size of turbinates.



ALLERGIC RHINITIS

Definition: Allergic rhinitis (AR) is an immunoglobulin E (IgE)-mediated inflammatory nasal condition resulting from allergen exposure in a sensitized individual. Allergic rhinitis is a common inflammatory condition of the URTI, characterized by nasal pruritus, sneezing, rhinorrhea, and nasal congestion. Frequently, there is associated palate, throat, ear, and eye itching as well as eye redness, puffiness, and watery discharge.

Etiology: type-I hypersensitivity reaction (an IgE-mediated process)

Risk factor: family history of allergy or atopy, age <20 years, exposure to aeroallergens such as plant pollens (grasses, trees, weeds), molds spores, house dust mites, cockroaches, latex, pollution)

CLINICAL CLASSIFICATION OF ALLERGIC RHINITIS

Classification criteria		Definition
Temporal pattern of allergen exposure	Episodic allergic rhinitis	Symptoms occur on exposure to allergens that are not normally a part of the individual's environment
	Seasonal allergic rhinitis	Symptoms occur on exposure to allergens that occur during particular seasons.
	Perennial allergic rhinitis	Symptoms occur on exposure to allergens that are normally a part of the patient's environment
Frequency	Intermittent allergic rhinitis	Duration of symptoms: < 4 days/week or < 4 weeks/year
	Persistent allergic rhinitis	Duration of symptoms: > 4 days/week for > 4 weeks/year
Severity	Mild allergic rhinitis	Symptoms do not interfere with the quality of life.
	Moderate to severe allergic rhinitis	Symptoms interfere with the quality of life.

Clinical features

- Recurrent episodes of:
 - Nasal pruritus
 - Sneezing
 - Rhinorrhea
 - Nasal congestion
 - Post-nasal drip
- Associated symptoms:** Itching of palate, throat, ear, and itchy eyes, Eye redness (Conjunctival conjuction), puffiness, and watery discharge.
- Constitutional symptoms:** Fatigue, Irritability.
- Associated allergic conditions**
 - Allergic conjunctivitis
 - Atopic dermatitis &/or bronchial asthma
- Physical exam of the nose:** may include swelling of the turbinates and nasal mucosa, the presence of clear nasal mucus and/or a pale nasal mucosa, and nasal crease (a transverse crease resulting from repetitive nose rubbing and manipulation).
- Physical exam of the face:** may identify allergic shiners (bluish discoloration in the infraorbital region), conjunctival injection, ocular mucoid discharge, and, less commonly, Dennie-Morgan lines (creases present under the lower eyelids).

Diagnostic workup

- Clinical diagnosis
- Clinical improvement of Therapeutic trial with antihistamine + intranasal steroids
- Allergy testing:** allergen skin prick test, total IgE level, RAST test, basophil activation test (BAT)

TREATMENT OF ALLERGIC RHINITIS

- Allergen avoidance:** advice patient to avoid exposure to allergen is one of the guiding principles of treatment.
- Intranasal steroids:** In patients with mild or intermittent symptoms, intranasal corticosteroids are a first-line treatment.
 - Fluticasone 50mcg nasal spray (Flixonase or Ticovate) 1-2 sprays in each nostril twice daily
 - OR Mometasone nasal spray (Rinelon or Hivate) x 2-3 in sprays in each nostril twice daily.
- 2nd gen. Antihistamine:** **Treatment duration 5-7 days**
 - Tab. Cetirizine 10mg (T-day, Zyrtec, Rigix) x OD
 - OR Tab. Desloratidine 5mg (Desora, Jordin-D) x OD
 - OR Tab. Fexofenadine 180mg (Telfast, Fexo) x OD
 - OR Tab. Levocetirizine 5mg (Belair, T-day) x OD
 - 0 - 0 - 1 (Orally once daily (OD) when required)
- Intranasal antihistamine** are another first-line option when symptoms are intermittent and do not require daily medication, If symptoms are persistent, an intranasal corticosteroid and intranasal antihistamine may be continued in combination.
 - Azelastine 0.1% nasal spray (Azosin)x 1-2 sprays in each nostril once to twice daily
 - Olopatadine 0.6% nasal spray (Olonase) x 2 sprays in each nostril twice daily
- N.B. Excessive use of nasal drops and sprays should be avoided because it may lead to rhinitis medicamentosa
- Referral to ENT specialits for allergen immunotherapy

DEVIATED NASAL SEPTUM (DNS)

Definition: significant displacement of the nasal septum from the midline that often leads to nasal airway obstruction

Etiology

- » Congenital: due to growth disturbances or intrauterine conditions resulting in pressure on the facial bones
- » Traumatic: e.g., septal hematoma due to facial and/or nasal fractures
- » Iatrogenic: septoplasty/rhinoplasty, obstetric forceps delivery

Types of DNS: Deviation may involve only the cartilage, bone or both the cartilage and bone.

1. **Anterior dislocation:** Septal cartilage may be dislocated into one of the nasal chambers. This is better appreciated by looking at the base of nose when patient's head is tilted backwards
2. **C-shaped deformity:** Septum is deviated in a simple curve to one side. Nasal chamber on the concave side of the nasal septum will be wider and may show compensatory hypertrophy of turbinates.
3. **S-shaped deformity:** Either in vertical or anteroposterior plane → may cause bilateral nasal obstruction.
4. **Spurs:** A spur is a shelf-like projection often found at the junction of bone and cartilage. A spur may press on the lateral wall and gives rise to headache. It may also predispose to repeated epistaxis from the vessels stretched on its convex surface
5. **Thickening:** It may be due to organized haematoma or overriding of dislocated septal fragments.

Clinical features

- » Difficulty breathing (typically in only one nostril)
- » Nasal congestion/obstruction
- » Snoring or noisy breathing during sleep
- » Headaches or facial pain
- » Sinusitis: Deviated septum may obstruct sinus ostia resulting in poor ventilation of the sinuses.
- » Epistaxis (nosebleeds)
- » Anosmia: Failure of the inspired air to reach the olfactory region may result in total or partial loss of sense of smell.
- » External deformity
- » Middle ear infection: DNS also predisposes to middle ear infection.

Diagnostic workup

- » Anterior rhinoscopy and/or nasal endoscopy: a nasal speculum and external light source are used to visualize the septum.
- » CT PNS/Cranial: for more detailed evaluation of the nasal septum and adjacent structures.

Surgical Approaches

- » **Septoplasty:** a preferred surgical procedure that corrects a deviation of the bone or cartilage of the nasal septum
- » **Submucous resection (SMR) operation:** Here apart from a thin dorsal and caudal strip, the rest of the entire septum is removed. It is generally done in adults under local anaesthesia.
- » **N.B.** Septal surgery is usually done after the age of 17 so as not to interfere with the growth of nasal skeleton. Only if a child has severe septal deviation causing marked nasal obstruction, septoplasty should be done.

Cranial CT scan (Coronal section): shows deviation of the nasal septum (blue overlay) to the left is visible as well as compensatory hypertrophy of the right middle and inferior turbinates (yellow overlay).



TREATMENT OF DEVIATED NASAL SEPTUM

Usually treatment not is required, if it is not causing any symptoms. Give symptomatic or correct underlying cause

» Nasal saline irrigations/sprays for symptomatic relief:

- ↳ Nosaline-P drops x 2-3 sprays/drops into each nostril every 2 to 4 hours.

» **Intranasal steroids:** Fluticasone 50mcg nasal spray (Flixonase or Ticovate) 1-2 sprays in each nostril twice daily OR Mometasone nasal spray (Rinelon or Hivate) x 2-3 in sprays in each nostril twice daily.

» **2nd generation Antihistamine:**

- ↳ OR Tab. Desloratidine 5mg (Desora, Jordin-D) x OD
- ↳ OR Tab. Fexofenadine 180mg (Telfast, Fexo) x OD
- ↳ OR Tab. Levocetirizine 5mg (Belair, T-day) x OD

» **Analgesia/Headache/Facial pain**

- ↳ Tab. Tab. Diclofenac sodium 50mg (Voren) x BD
- ↳ OR Tab. Paracetamol 500mg (Panadol, Calpol) at dose 500mg-1000mg x three times a day.

» Treat with antibiotics sinus infection see chronic sinusitis



SEPTAL HAEMATOMA

Name:	Age:	Sex:	Date:
Temperature:	B.P:	Pulse:	Resp. Rate:

It is collection of blood under the perichondrium or periosteum of the nasal septum
It often results from nasal trauma or septal surgery. In bleeding disorders, it may occur spontaneously.

△
C/C:

- » Bilateral nasal obstruction is the commonest presenting symptom.
- » This may be associated with frontal headache and a sense of pressure over the nasal bridge.
- » Examination reveals smooth rounded swelling of the septum in both the nasal fossae.
- » Palpation may show the mass to be soft and fluctuant.

Duration of treatment: 5 days

COMPLICATIONS

Septal haematoma, if not drained, may organize into fibrous tissue leading to a permanently thickened septum. If secondary infection supervenes, it results in septal abscess with necrosis of cartilage and depression of nasal dorsum.

Rx

- » Small haematomas can be aspirated with a wide bore sterile needle.
- » Larger haematomas are incised and drained by a small anteroposterior incision parallel to the nasal floor.
- » Excision of a small piece of mucosa from the edge of incision gives better drainage.
- » Following drainage, nose is packed on both sides to prevent re-accumulation.
- » Systemic antibiotics should be given to prevent septal abscess.

1. Tab. Co-Amoxiclave 625mg (Augmentin, Calamox)
1 - 1 - 1 (TDS)
OR Tab. Co-Amoxiclave 1g (Augmentin, Calamox)
OR Cap. Cefixime 400mg (Cefspan, Cefim)
0 - 0 - 1 (OD)
2. Tab. Mefenamic acid 500mg (Ponstan fort, Mefnac DS)
1 - 1 - 1 (TDS)

SEPTAL ABSCESS

Name:	Age:	Sex:	Date:
Temperature:	B.P:	Pulse:	Resp. Rate:

Septal abscess mostly, it results from secondary infection of septal haematoma. Occasionally, it follows furuncle of the nose or upper lip. It may also follow acute infection such as typhoid or measles

△

C/C:

- » Severe B/L nasal obstruction with pain and tenderness over the bridge of nose.
- » Patient may also complain of fever with chills and frontal headache. Skin over the nose may be red and swollen.
- » Internal examination of nose reveals smooth bilateral swelling of the nasal septum, Fluctuation can be elicited in this swelling.
- » Septal mucosa is often congested. Submandibular lymph nodes may also be enlarged and tender.

Rx

- » Abscess should be drained as early as possible. Incision is made in the most dependent part of the abscess and a piece of septal mucosa excised.
- » Pus and necrosed pieces of cartilage are removed by suction. Incision may require to be reopened daily for 2-3 days to drain any pus or to remove any necrosed pieces of cartilage.
- » Systemic antibiotics are started as soon as diagnosis has been made & continued at least for a period of 10 days



NASAL TURBINATE HYPERTROPHY

Name:	Age:	Sex:	Date:
Temperature:	B.P:	Pulse:	Resp. Rate:
Etiology: Allergic rhinitis, Infection (e.g., nasopharyngitis), Deviated nasal septum, Rhinitis medicamentosa			
Clinical features		TREATMENT OF NASAL TURBINATE HYPERTROPHY	
» Nasal congestion with difficulty breathing through the nose » Acute or recurrent sinusitis » Snoring » Headaches and facial pain		Rx » Analgesia for headache/facial pain ↳ Tab. Tab. Diclofenac sodium 50mg (Voren) x BD/TDS OR Tab. Paracetamol 500mg (Panadol, Calpol) at dose 500mg-1000mg x three times a day. » Nasal saline irrigations/sprays for symptomatic relief: ↳ Norsaline-P drops x 2-3 sprays/drops into each nostril every 2 to 4 hours. » Intranasal steroids: Fluticasone 50mcg nasal spray (Flixonase or Ticovate) 1-2 sprays in each nostril twice daily OR Mometasone nasal spray (Rinelon or Hivate) x 2-3 in sprays in each nostril twice daily. » 2 nd generation Antihistamine: ↳ OR Tab. Desloratidine 5mg (Desora, Jordin-D) x OD ↳ OR Tab. Fexofenadine 180mg (Telfast, Fexo) x OD ↳ OR Tab. Levocetirizine 5mg (Belair, T-day) x OD	
Diagnostic workup			
» Anterior rhinoscopy and nasal endoscopy: turbinate hypertrophy » X-ray PNS: initial test » CT scan PNS: indicated if rhinoscopy and nasal endoscopy are inconclusive.			

ADULT WITH EAR DISCHARGE/INFECTION

	Age:	Sex:	Date:
Temperature:	B.P:	Pulse:	Resp. Rate:
△ C/C: » Ear Pain » Ear Discharge » Fever » Headache Duration: 5-7 days			
Rx Prescription #1 » Analgesia/antipyretic: for headache, pain, fever ↳ Tab. Tab. Diclofenac sodium 50mg (Voren) x BD/TDS OR Tab. Aceclofenac 100mg (Acenac, Acelo) x BD OR Tab. Mefenamic acid 500mg (Ponstan fort, Mefnac DS) x TDS OR Tab. Paracetamol 500mg (Panadol, Calpol) at dose 500mg-1000mg x three times a day. » Antibiotic therapy for at least 7 – 10 days ↳ Tab. Co-Amoxiclavate 625mg (Augmentin, Calamox) x TDS ↳ OR Tab. Cefuroxime axetil 250mg (Zinacef) x BD ↳ OR Cap. Doxycycline 100mg (Doxyn, Vibramycin) x BD ↳ OR Tab. Clarithromycin XL 500mg (Klaricid XL) x OD ↳ OR Tab. Levofloxacin 500mg (Cravit, Levoxin) x OD ↳ OR Tab. Moxifloxacin 400mg (Maxlox, Xefecta, Avelox) x OD » Polymyxin + Lidocaine Ear drops (Otocain, Lidosporin) OR Polymyxin + Neomycin + Hydrocortisone Ear drops (Otosporin) 2-3-drops 3-4 time a day OR Tobramycin + Dexamethasone Ear drops (Dexatob 0.3%, Dexatob 0.6%) OR Ciprofloxacin + Lidocaine Ear drops (Cipocain, Zeprocaine) OR Ciprofloxacin + Dexamethasone Ear drops (Cipotic-D, Dexcip) 3-4 drops into effected ear x Twice or thrice a day.			

ACUTE SUPPURATIVE OTITIS MEDIA (ASOM)

Name:	Age:	Sex:	Date:
Temperature:	B.P.:	Pulse:	Resp. Rate:

Definition: Acute suppurative otitis media (ASOM) is an acute inflammation of middle ear cleft < 3 weeks, infective in origin, occurs in first 2 years of life. ASOM is one of the most common infectious disease seen in children

Route of infection: Most common is through Eustachian tube

Etiology:

- » **Bacterial:** Streptococcus pneumoniae (Most common), H. influenzae (2nd most common), Moraxella catarrhalis
- » **Viral:** Syncytial virus, Influenza virus, Rhino and adeno virus

Stages of ASOM

1. Stage of tubal occlusion
2. Stage of pre-suppurative
3. Stage of suppuration
4. Stage of resolution
5. Stage of complication

Diagnostic approach

Clinical diagnosis – investigation initially not required

Pneumatic otoscopy – findings

- » Bulging tympanic membrane (TM) with loss of landmarks
- » Opacification and loss of light reflex
- » Retracted and hypomobile tympanic membrane (TM)
- » Purulent/serosanguinous discharge in the external auditory canal or visible perforation
- » Distinct erythema of the tympanic membrane (TM)
- » **Additional findings that may be present:**
 - » Yellow spot on the tympanic membrane (TM)
 - » Cartwheel tympanic membrane (TM)
 - » Blisters/bullae on the tympanic membrane (TM)

Tuning fork test:

- » The Weber test and Rinne test can be performed to verify conductive hearing loss secondary to an effusion.
 - » **Weber test:** Sound localizes to the affected ear.
 - » **Rinne test:** Air conduction is impaired in the affected ear, while bone conduction remains intact.

CBC: Leukocytosis maybe present

Gram stain and culture of middle ear fluid – if patient not responded to treatment

Blood cultures: indicated only in severe infection

Clinical features

- » **Ear pain (Otalgia)**, described as throbbing pain in Adults most frequently report
- » Preceding by upper respiratory symptoms
- » Fever, irritability, sleep disturbance
- » Otorrhea (Ear discharge) in the case of a ruptured tympanic membrane.
- » Erythema, redness and inflammation of the tympanic membrane
- » Hearing loss in the affected ear

Unresponsive to treatment:

- » **Tympanocentesis:** can relieve pressure in the middle ear space and provide relief from otalgia. This procedure may benefit patients with persistent disease unresponsive to antimicrobial therapy or those in need of immediate pain relief.
- » Tympanocentesis involves risks including trauma to the tympanic membrane and middle ear structures, as well as risks associated with anesthesia.

**TREATMENT OF ACUTE SUPPURATIVE OTITIS MEDIA**

Analgesia/antipyretic: for headache, pain, fever

- » **Tab. Diclofenac sodium 50mg (Voren)** x BD/TDS
- OR **Tab. Aceclofenac 100mg (Acenac, Acelo)** x BD
- OR **Tab. Paracetamol 500mg (Panadol, Calpol)** at dose 500mg–1000mg x three times a day.

Antibiotic therapy for at least 7 – 10 days

- » **Tab. Co-Amoxiclav 625mg (Augmentin, Calamox)** x TDS
- » OR **Tab. Cefuroxime axetil 250mg (Zinacef)** x BD
- » OR **Cap. Doxycycline 100mg (Doxyn, Vibramycin)** x BD
- » OR **Tab. Clarithromycin XL 500mg (Klaricid XL)** x OD
- » OR **Tab. Levofloxacin 500mg (Cravit, Levoxin)** x OD
- » OR **Tab. Moxifloxacin 400mg (Maxlox, Xefecta)** x OD

Polymyxin + Lidocaine Ear drops (Otocain)

- OR **Ciprofloxacin + Lidocaine Ear drops (Cipocain)**
- 3-4 drops into effected ear x Twice or thrice a day.

No sufficient evidence to support the routine use of opioids, decongestants, antihistamines, steroids



CHRONIC SUPPURATIVE OTITIS MEDIA (CSOM)

Name:	Age:	Sex:	Date:
Temperature:	B.P:	Pulse:	Resp. Rate:

Definition: CSOM is chronic infection of the middle ear and mastoid. It is characterized by a permanent perforation in tympanic membrane. Generally, a perforation of tympanic membrane heals by 6-12 weeks. Therefore any perforation which persists for > 12 weeks is considered as permanent and leads to CSOM.

TYPES OF CSOM

Clinically, it is divided into two types:

1. **Tubotympanic:** Also called the safe or benign type; it involves anteroinferior part of middle ear cleft, i.e. eustachian tube and mesotympanum and is associated with a central perforation. Most common organisms isolated are - *P. aeruginosa*, *S. aureus* and *proteus* species. Here perforation occurs in any part of pars tensa except margins. There is no risk of serious complication. Most common in children.
2. **Atticoantral:** Also called unsafe or dangerous type; it involves postero-superior part of the cleft (i.e. attic, antrum and mastoid) and is associated with an attic or a marginal perforation. The disease is often associated with a bone eroding process such as cholesteatoma, granulations or osteitis. Risk of complications is high in this variety.

Complications: In long standing cases of Tubotympanic variety of CSOM, necrosis of ossicles can occur due to repeated infection. The Most common ossicle to necrosis is Incus (long process)

Differences between tubotympanic and atticoantral type of CSOM

Features	Tubotympanic or safe type	Atticoantral or unsafe type
Discharge	Profuse, mucoid, odourless	Scanty, purulent, foul smelling
Perforation	Central	Attic or marginal
Granulations	Uncommon	Common
Polyp	Pale	Red and fleshy
Cholesteatoma	Absent	Present
Complications	Rare	Common
Audiogram	Mild to moderate conductive deafness	Conductive or mixed deafness

△ Tubotympanic type of CSOM C/C:

- » **Ear discharge:** It is non-offensive, mucoid or mucopurulent, constant or intermittent. The discharge appears mostly at time of upper RTI or on accidental entry of water into the ear.
- » **Conductive type hearing loss**
- » **Perforation:** always central, it may lie anterior, posterior or inferior to the handle of malleus. It may be small, medium or large or extending up to the annulus, i.e. subtotal
- » **Middle ear mucosa:** seen when the perforation is large



TREATMENT OF TUBOTYMPANIC TYPE OF CSOM

Medical treatment: Treatment of Choice

- » **Aural toilet:** Important step in treatment & should not be missed.
 - » Remove all discharge and debris from the ear.
 - » It can be done by dry mopping with absorbent cotton buds, suction clearance under microscope or irrigation (not forceful syringing) with sterile normal saline.
 - » Ear must be dried after irrigation.
- » **Topical ear drops:**
 - » Ciprofloxacin + Lidocaine Ear drops (Cipocain)
 - » OR Ciprofloxacin + Dexamethasone Ear drops (Cipotic-D)
 - » OR Tobramycin + Dexamethasone Ear drops (Dexatob) x 3-4 drops into effected ear x twice or thrice a day.
- » **Systemic antibiotics:** Limited role, can be given in early, acute cases
 - » Tab. Co-Amoxiclav 625mg (Augmentin, Calamox) x TDS
 - » OR Tab. Cefuroxime axetil 250mg (Zinacef) x BD
 - » OR Cap. Doxycycline 100mg (Doxyn, Vibramycin) x BD
 - » OR Tab. Clarithromycin XL 500mg (Klaricid XL) x OD
 - » OR Tab. Levofloxacin 500mg (Cravit, Levoxin) x OD

△ Atticoantral type of CSOM

- C/C:**
- **Ear discharge:** Usually scanty, but always foul-smelling due to bone destruction.
 - **Hearing loss:** Hearing is normal when ossicular chain is intact or when cholesteatoma, having destroyed the ossicles, bridges the gap caused by destroyed ossicles (cholesteatoma hearer). Hearing loss is mostly conductive but sensorineural element may be seen
 - **Bleeding:** may occur from granulations or the polyp when cleaning the ear.
 - **Perforation:** Either attic or posterosuperior marginal type
 - **Retraction pocket:** An invagination of tympanic membrane is seen in the attic or posterosuperior area of pars tensa. Degree of retraction and invagination varies. In early stages, pocket is shallow and self-cleansing but later when pocket is deep, it accumulates keratin mass and gets infected
 - **Cholesteatoma:** Pearly-white flakes of cholesteatoma can be sucked from the retraction pockets.

- **Precautions:** Patients are instructed to keep water out of the ear during bathing, swimming and hair wash. Rubber inserts can be used. Hard nose blowing can also push the infection from nasopharynx to middle ear and should be avoided
- **Treatment of contributory causes:** Attention should be paid to treat concomitantly infected tonsils, adenoids, maxillary antra and nasal allergy.

Surgical treatment

Surgical treatment is done at a later stage to correct the hearing loss

• Prerequisites

- Ear dry for 6 weeks without antibiotics
- Eustachian tube function normal
- Normal middle ear mucosa

• Procedure of choice:

- Myringoplasty - if ossicle chain is intact
- Tympanoplasty - if ossicular chain is disrupted



TREATMENT OF ATTICOANTERAL TYPE OF CSOM

Surgical: It is the mainstay of treatment.

- Primary aim is removal of disease by mastoidectomy to make ear safe followed by reconstruction of hearing at a later stage.
- **Two types of surgical procedures are done to deal with cholesteatoma:**
 - » Canal wall down procedures.
 - » Canal wall up procedures.
- **Surgery of choice:** Modified Radical mastoidectomy

COMPARISON OF CANAL WALL UP AND CANAL WALL DOWN PROCEDURES

Features	Canal wall up procedure	Canal wall down procedure
• Meatus	Normal appearance	Widely open meatus communicating with mastoid
• Dependence	Does not require routine cleaning	Dependence on doctor for cleaning mastoid cavity once or twice a year
• Recurrence or residual disease	High rate of recurrent or residual cholesteatoma	Low rate of recurrence or residual disease and thus a safe procedure
• Second look surgery	Requires second look surgery after 6 months or so to rule out cholesteatoma	Not required
• Patients limitations	No limitation. Patient allowed swimming	Swimming can lead to infection of mastoid cavity and it is thus curtailed
• Auditory rehabilitation	Easy to wear a hearing aid if needed	Problems in fitting a hearing aid due to large meatus and mastoid cavity which sometimes gets infected



OTITIS EXTERNA

Name:	Age:	Sex:	Date:
Temperature:	B.P.:	Pulse:	Resp. Rate:

ETIOLOGY

Infectious causes

- » **Bacterial infections** (most common cause of otitis externa)
Pseudomonas aeruginosa (= 40%), commonly from swimming activities. *Staphylococcus aureus*, *Proteus mirabilis*, *Escherichia coli* but more often the infection is mixed.

- » **Viral infections (rare):** Herpes zoster, influenza viruses

- » **Fungal infections (less common):** *Aspergillus niger* (90%), *Candida*

Non-infectious causes (part of generalized skin condition) – less common

- » Seborrheic otitis externa (associated with seborrheic dermatitis)
- » Eczematous otitis externa (a HSR to pathogens or topical antibiotics)
- » Neurodermatitis (caused by compulsive/psychogenic scratching).
- » Psoriasis

Risk factors

- » Trauma to external ear canal
- » Vigorous cleaning of ear canal
- » Scratching the ear canal with hair pins or matchsticks
- » Insertion of foreign objects
- » Increased moisture in the external auditory canal (EAC) (swimming, humid climate)
- » **Immunosuppression:**
 - Diabetes mellitus
 - HIV

CLASSIFICATION OF OTITIS EXTERNA

- » Localized acute otitis externa (Furunculosis)
- » Diffuse otitis externa
- » Malignant otitis externa (Necrotizing otitis externa)
- » Otomycosis
- » **Other:** Otitis externa hemorrhagica, herpes Zoster oticus, Eczematous OE, Part of generalized skin condition

LOCALIZED ACUTE OTITIS EXTERNA (FURUNCULOSIS)

- » **Most common organism:** *Staphylococcus aureus* (other less common may be Group A *Streptococcus*)
- » **Site:** Hair bearing area of the cartilaginous part of the external auditory canal

△ Localized acute otitis externa
C/C:

Symptoms:

- » Discomfort and severe pain
- » Pain is aggravated by jaw/pinna movement in chewing
- » May have associated deafness/hearing loss if canal gets occluded due to edema

Signs:

- » Tenderness on pressing of the tragus (Tragal sign positive)
- » **In severe cases:**
 - Retroauricular sulcus is obliterated
 - Forward displacement of the pinna
 - Periauricular lymph nodes may be enlarged and tender.

Treatment duration: 7 days, maybe extended up to 10-14 days.



Treatment of Localized acute otitis externa

Treatment in early cases, without abscess formation, consists of systemic antibiotics, analgesics and local heat.

- » **Local – 10% ichthammol glycerin ear pack:** Provides splintage and reduces pain. Hygroscopic action of glycerine reduces oedema, while ichthammol is mildly antiseptic.
- » **Combination of topical Antibiotics with corticosteroids**
 - ↳ **Ciprofloxacin + Dexamethasone Ear drops** (Cipotec-D) 3-4 drops into effected ear x Twice or thrice a day.
- » **Consider oral Antibiotics:** if local cellulitis is present (if disease extension outside the ear canal, locally involvement)
 - ↳ **Tab. Co-Amoxiclav 1g** (Augmentin, Calamox) x BD
 - OR **Cap. Cephalexin 500mg** (Ceporex, Keflex) x BD
 - OR **Cap. Cefadroxil 500mg** (Duricef, Cedrox) x BD
- » **Analgesia/pain relief:**
 - ↳ **Tab. Paracetamol 500mg** (Calpol, Panadol) x TDS
 - OR **Tab. Diclofenac sodium 50mg** (Voren, Voltrel) x BD
 - OR **Tab. Aceclofenac 100mg** (Acenac, Alkeris) x BD
- » Incision and drainage – If abscess formation
- » In recurrent furunculosis – Rule out diabetes mellitus
- » In case of recurrent furunculosis, diabetes should be excluded, should be treated with specific antibiotics according discharge culture, if present.



DIFFUSE OTITIS EXTERNA

- Definition: It is diffuse inflammation of meatal skin which may spread to involve the pinna and epidermal layer of tympanic membrane. Disease is commonly seen in hot and humid climate and in swimmers.
- Also known as Tropical or Singapore ear or Telephonist ear or swimmer ear
- Most common organism: *Pseudomonas aeruginosa*
- Other: *Staphylococcus aureus*, *Proteus mirabilis*, *Escherichia coli* but more often the infection is mixed.
- Two types:
 - Acute: inflammation of the external auditory canal (EAC) lasting < 6 weeks.
 - Chronic: inflammation of the external auditory canal (EAC) lasting at least 6 weeks to 3 months.

△ Diffuse otitis externa

C/C:

Acute phase is characterized by hot burning sensation in the ear, followed:

- Severe ear pain, particularly at night radiating to jaw (Jaw pain)
- Intense itching in the EAC
- Ear starts oozing thin serous discharge which later becomes thick and purulent.
- Meatal lining becomes inflamed & swollen
- Hearing loss

Chronic phase is characterized by:

- Irritation & constant desire to itch.
- Scanty discharge in the EAC
- Dried crust
- Meatal skin which is thick and swollen may also show scaling and fissuring.
- Rarely, the skin becomes hypertrophic leading to meatal stenosis (chronic stenotic otitis externa)

Examination findings

- Tenderness on pressing of the tragus (Tragal sign positive)
- Pulling up & back on the auricle causes pain
- The following may also be present:
 - Dried ear discharge
 - Collection of debris and discharge accompanied with meatal swelling
 - Conductive hearing loss
 - Severe cases: Regional lymphadenitis with cellulitis of surrounding tissues

Otoscopy

- Erythematous and edematous external auditory canal (EAC)
- Otorrhea or debris
- EAC may be occluded by a furuncle, impacted cerumen, or foreign body
- The tympanic membrane may be erythematous but should not bulge.



TREATMENT OF DIFFUSE OTITIS EXTERNA

Treatment of Acute phase is treated as follows:

- Ear toilet:** It is the most important single factor in the treatment of diffuse otitis externa. All exudate and debris should be meticulously and gently removed. Special attention should be paid to anteroinferior meatal recess, which forms a blind pocket where discharge is accumulated. Ear toilet can be done by dry mopping, suction clearance or irrigating the canal with warm, sterile normal saline
- Medicated wicks:** After thorough toilet, a gauze wick soaked in antibiotic steroid drops (Cipotec-D) is inserted in the ear canal & patient advised to keep it moist by instilling the same drops 3-4 drops twice or thrice a day. Wick is changed daily for 2-3 days when it can be substituted by ear drops.
- Oral antibiotics:** indicated in case of cellulitis & lymphadenitis
 - Tab. Ciprofloxacin 750mg (Hiflox, Quinoflox) x BD
 - OR Tab. Levofloxacin 750mg (Leflox, Levoxin) x OD
- Consider one of the following; if discharge culture positive for mixed coinfection infection:**
 - Tab. Co-Amoxiclav 1g (Augmentin, Calamox) x BD
 - OR Tab. Cefuroxime 250mg (Zinacef, Zecef) x 500mg x BD
- Oral Analgesics for pain relief:**
 - Tab. Diclofenac sodium 50mg (Voren, Voltral) x BD
 - OR Tab. Aceclofenac 100mg (Acenac, Alkeris) x BD
- Consider Gastroprotective – PPIs (Omeprazole, Esomeprazole)**
 - Cap. Omeprazole 40mg (Omega, Ruling) x OD
 - OR Cap. Esomeprazole 40mg (Esso, Eskem) x OD

Chronic phase:

- Treatment aims at:** 1. Reduction of meatal swelling so that ear toilet can be effectively done. 2. Alleviation of itching so that scratching is stopped and further recurrences controlled.
- A gauze wick soaked in 10% ichthammol glycerine and inserted into the canal helps to reduce swelling. This is followed by ear toilet with particular attention to anteroinferior meatal recess. Itching can be controlled by topical application of antibiotic steroid cream (Betnovate-N cream or Betaderm-N).
- When the meatal skin is thickened to the point of obstruction and resists all forms of medical treatment, i.e. chronic stenotic otitis externa, it is surgically excised, bony meatus is widened with a drill and lined by split skin graft.



MALIGNANT OTITIS EXTERNA (NECROTIZING OTITIS EXTERNA)

- ☛ **Definition:** Progressive debilitating and sometimes fatal infection of the external auditory canal, characterized by granulation tissue in external auditory canal at the junction of bone and cartilage
- ☛ **Most common organism:** *Pseudomonas aeruginosa*
- ☛ **Other organism:** *Staphylococcus aureus*, *S. epidermidis*, *Aspergillus*, *Actinomyces*
- ☛ **Risk factors:** Occurs commonly in
 - » Elderly diabetic patient
 - » Immunosuppressed patient/use of immunosuppressive drugs
 - » Patients who have received radiotherapy to skull base

Diagnostic workup

- ☛ Severe otalgia in an elderly diabetic patient with granulation tissue in the external ear canal at its cartilaginous-bony junction should alert the physician of necrotizing otitis externa.
- ☛ **Investigation:** CT scan, gallium and technetium-99 scintigraphy
 - » **For early diagnosis:** **Technetium 99 bone scan** reveals bone infection but test remains positive for a year or so, hence cannot be used to monitor the disease
 - » **For monitoring the disease:**
 - ☛ **Gallium-67 scan:** Most useful in diagnosis and follow-up of the patient. It is taken up by monocytes and reticuloendothelial cells, and is indicative of soft tissue infection. It can be repeated every 3 weeks to monitor the disease and response to treatment.
 - ☛ **Indium (in III) labelled leucocyte scan** is equally sensitive but more specific than **Gallium-67 scan**
 - » **CT scan and MRI** are equally sensitive to assess the extent of disease (show bony destruction) but MRI is more sensitive for detecting intracranial complication.
 - » **Culture and sensitivity**
 - » **Biopsy** is done to rule out malignancy
 - » **Serum ESR** is often raised and can be used to monitor the progress of disease

△ Malignant (Necrotizing) otitis externa C/C:

- » Early manifestations resemble diffuse otitis externa but there is excruciating pain and appearance of granulations in the ear canal.
- » Most commonly damage facial nerve (CN VII) which lead to facial paralysis
- » Infection may spread to the skull base and jugular foramen causing multiple cranial nerve palsies (CN IX, X, XI, XII)
- » Anteriorly, infection spreads to temporo-mandibular fossa, posteriorly to mastoid and medially into the middle ear & petrous bone.

Prognosis:

- » It has high mortality rate (So termed as malignant)
- » Death due to intracranial complications like sigmoid sinus thrombosis

Rx

Treatment of malignant (necrotizing) otitis externa

- ☛ Correction of immunosuppression (when Possible)
- ☛ Control of diabetes, according HBA1C guidelines
- ☛ **Ear canal toilet:** Remove discharge, debris and granulations or any dead tissue or bone – biopsy sent for culture in all cases
- ☛ **Antibiotic treatment:** against causative organism, according culture and sensitivity. Antibiotic treatment is continued for 6-8 weeks, sometimes more.

Intravenous antibiotics:

- ☛ **Inj. Ceftriaxone 2g** (Oxidil, Rocephin) 1-2g/day x BD
OR **Inj. Ceftazidime 1g** (Fortum, Fortazim) 1-2g/day IV x BD
OR **Inj. Piperacillin/tazobactam 4.5g** (Tanzo, Tazocin) x TDS
OR **Inj. Meropenem 1g** (Merpen, Meronem) x TDS

Plus one of the following:

- ☛ **Tab. Ciprofloxacin 750mg** (Hiflox, Quinolox) x BD
OR **Tab. Levofloxacin 750mg** (Leflox, Levoxin) x OD
- ☛ Prolonged antibiotic treatment has replaced radical surgery and resections done earlier for this condition.
- ☛ Ear drops containing antipseudomonal antibiotic e.g. ciprofloxacin plus a glucocorticoid is also used.

- ☛ For *Pseudomonas aeruginosa*: The regimen involves an antipseudomonal penicillin (Piperacillin/tazobactam) or 3rd gen. cephalosporin (Ceftriaxone, ceftazidime) with an aminoglycoside (Amikacin, Gentamicin).
- ☛ Fluoroquinolone (Ciprofloxacin, Levofloxacin) can be used in place of the aminoglycoside (Amikacin, Gentamicin)



OTOMYCOSIS (FUNGAL OTITIS EXTERNA)

- Definition: Otomycosis (or fungal Otitis externa) is a fungal infection in the outer ear canal. Chronic and recurrent Otomycosis is frequently seen in Diabetic and elderly patients.
- Most common organism: *Aspergillus niger* > candida
- Others organism: *Aspergillus Fumigatus*, Dermatophytes (*Actinomyces*)
- Risk factors
 - Immunosuppression: Diabetes mellitus, HIV infection
 - Long-term antibiotic and steroid therapy
 - Residence in a Hot and Humid climatic condition

△ Otomycosis

C/C:

- Intense itching
- Discomfort or pain in the ear
- Watery discharge with musty odour and ear blockage
- Thick debris in the ear canal
- Visible hyphae
- Insufficient response to antimicrobial therapy

Otoscopy

- Aspergillus niger*: Appear as black-headed filamentous growth
- Candida albicans*: Appear as white and creamy deposit
- Aspergillus fumigatus*: Appear as pale blue or green
- Dermatophytes: *Actinomyces* (Wet blotting paper appearance)

Swabs from infected ear: Fungal culture, Bacterial culture, KOH

Rx

TREATMENT OF OTOMYCOSIS

- Debridement & cleaning:** Ear toilet to remove all discharge & epithelial debris which are conducive to the growth of fungus.
 - It can be done by syringing, suction or mopping.
 - Cleaning may be required several times a week
 - Keep the ear dry & avoid scratching it with cotton wool buds.
- Topical Antifungal therapy:** Topical Clotrimazole 1% solution drops (Dermosporin, Clotrim) x Instill in affected 3-4 times a day for 7-10 days or till cure to avoid recurrences.
- Systemic antifungal:** effective against *Candida* and *Aspergillus*, with good penetration of bone and the CNS infections.
 - Cap. Itraconazole 100mg (Icon, Sporanox, Rolac) at dose 200mg (2 capsules) x Once daily for 5 days
- Antibiotic/steroid drops** helps to reduce inflammation and edema and thus permitting better penetration of antifungal agents.
 - Ciprofloxacin + Dexamethasone Ear drops (Cipotec-D) 3-4 drops into effected ear x Twice or thrice a day.

HERPETIC OTITIS EXTERNA

- Definition: It is characterized by formation of vesicles on the tympanic membrane, meatal skin, concha and postauricular groove. (Also known as Geniculate Herpes; Ramsay Hunt Syndrome; Viral Neuronitis)
- Most common viral organism: Herpes simplex, Herpes zoster

△ Herpetic otitis externa

C/C:

Clinical features of Herpes zoster/Ramsay Hunt syndrome

- Site of affection:
 - Geniculate ganglion of the facial nerve
 - May also involve the V and VIII nerves
- Symptoms:
 - Severe ear pain
 - Fluid-filled blisters (vesicles) on the outside of the ear (pinna) and in the ear canal
 - Facial nerve palsy (LMN type)
 - May show associated vesicular eruption in the buccal mucosa, hard palate and hypopharynx.

Rx

TREATMENT OF HERPETIC OTITIS EXTERNA

1. Tab. Prednisolone 5mg (Deltacortril, Rapicort) at dose 50 mg per orally daily for 10 days x 5 - 0 - 5 (5 tablets = 25mg)
2. Tab. Aciclovir 200mg or 400mg (Acylex, Zovirox)

Dosage: at dose 400mg x PO x 5 times daily for 10 days
OR 800mg x PO x 3 times daily for 5-10 days (to be started within 72 hours of the onset of rash)
3. Pain control: see post-herpetic neuralgia (PHN) - neurology
 - Tab. Carbamazepine 200mg (Tegral, Teril) x BD
 - OR Cap. Gabapentin 300mg (Gabix, Neogab) x BD
 - OR Tab. Amitriptyline 25mg (Tryptanol, Amyline) x BD
4. Consider Opioids: If Severe neuropathic pain
 - Tab. Tramadol 100mg (Tramal SR, Tonoflex SR) x BD



EAR WAX (CERUMEN IMPACTION)

Definition: Cerumen is a mixture of secretions and sloughed epithelial cells. A cerumen impaction is an accumulation of cerumen that causes symptoms, such as hearing loss, fullness, otorrhea, tinnitus, dizziness, or other symptoms, and/or prevents a required assessment of the ear canal, tympanic membrane, or audiovestibular system. While anyone can develop cerumen impaction.

Risk factors for cerumen impaction:

- » Anatomical abnormalities of the external auditory canal (e.g., ear canal stenosis)
- » **Regular use of foreign objects in the ear canal, e.g.:** Hearing aids, Earbud headphones, Cotton-tipped swabs or bobby pins for cleaning or scratching
- » Certain dermatological conditions (e.g., eczema, seborrheic dermatosis)
- » **Individuals who are unable to recognize or effectively communicate symptoms of cerumen impaction, such as:** older adults, especially those living in long-term care facilities, young children, individuals with cognitive impairment

Clinical features

- » **Localized symptoms:** Ear pain, itching and feeling of fullness, Otorrhea, Odor
- » **Hearing loss:** conductive hearing loss, decreased hearing aid performance
- » Cough, Tinnitus, vertigo
- » **Nonspecific symptoms** (more common in patients who are unable to communicate)
 - » Speech delay
 - » Behavioral changes
 - » Cognitive decline

Diagnostic workup

- » **Clinical diagnosis**
- » **Otoscopy findings:** tightly packed cerumen in the outer ear canal that partially or completely obstructs visualization of the auditory canal and/or tympanic membrane.



TREATMENT OF EAR WAX (CERUMEN IMPACTION)

Cerumen removal methods: Any of the following may be used alone or in combination unless there are contraindications for specific cerumen removal methods.

1. Cerumenolytic agents

- » Normal saline or water
- » OR Sodium bicarbonate 10% drops
- » OR Acetic acid otic 2% solution
- » OR Docusate sodium otic drops

Instill 5-10 drops twice a day for at least 3-15 days and then return for reexamination.

Contraindications: Children < 3 years of age, Possibility of a non-intact TM, Current otitis externa, Allergy to any ingredient in the cerumenolytic agent.

2. Ear canal irrigation

3. Manual cerumen removal

» Ear canal irrigation

- » Consider using a cerumenolytic agent 1-2 mL (20-40 drops) into the affected ear canal to soften and/or dissolve cerumen 15 minutes before irrigation.
- » **Method:** Water or saline that is close to body temperature is used to flush cerumen out of the **external auditory canal (EAC)** using a syringe (manual irrigation) or an electronic irrigator.
 - » Straighten the EAC by gently pulling the external ear in an upward and backward direction.
 - » An assistant holds a **receptacle (a kidney tray)** under the patient's ear to catch the irrigant.
 - » Gently instill the irrigant in the EAC, directing the fluid stream toward the wall of the EAC rather than toward the tympanic membrane; limit irrigation to < 30 minutes.
 - » Perform an otoscopy to ensure cerumen clearance and assess for complications.
 - » After irrigation, consider instilling hydrogen peroxide or acetic acid in the EAC to reduce the risk of infection (e.g., in individuals with diabetes).
- » **N.B.** Avoid using cold or warm irrigation fluids, as this may trigger caloric nystagmus & vertigo. In individuals with diabetes, avoid using tap water for irrigation as it may increase the risk of malignant otitis externa.

» Manual cerumen removal:

- » Should be performed in the clinic performed by a trained health care professional

» Method

- » Consider using a cerumenolytic agent 1-2 mL (20-40 drops) into the affected ear canal to soften and/or dissolve cerumen 15 minutes before irrigation.
- » An instrument (e.g., **curette, forceps, angulated suction tip**) is inserted into the ear canal to physically remove cerumen. Use an external light source to directly visualize the ear canal & cerumen during removal.

» **Unsuccessful removal:** Consider other cerumen removal methods and/or refer to ENT (otolaryngology).



TINNITUS

Tinnitus is a common condition in which sound (whistling, hissing, buzzing, ringing, and pulsating) is perceived in the absence of an external source. It can be unilateral or bilateral, acute or chronic, and intermittent or constant. Tinnitus is not a specific disease but a symptom that can be connected to a wide variety of etiologies, most commonly conditions associated with hearing loss.

Most people will experience tinnitus at some point in their lifetime.

Increases with age, More common in men and smokers

Associations: hearing loss, hyperacusis

Etiology

Tinnitus is a symptom, not a specific disease, and its presence can indicate an underlying abnormality.

Objective tinnitus: tinnitus that can be perceived by others, which is due to sounds created by the body (e.g., carotid artery stenosis, stapedial myoclonus)

Subjective tinnitus: tinnitus that is only perceived by the affected individual, which can be due to a wide range of etiologies (e.g., otosclerosis, tumor, infections, temporomandibular joint dysfunction)

△ Tinnitus**C/C:**

- Perceived sound without an external source (whistling, hissing, buzzing, ringing and pulsating)
- Symptoms of an underlying disease may be present as well (hearing loss)

Diagnosis

History: characterize the tinnitus (e.g., unilateral vs. bilateral, symptom duration, quality) and risk factors (sound exposure, chronic illness, and recent use of ototoxic medication)

Initial exam

- Otoscopic examination:** exclude infection, impacted cerumen
- Head and neck auscultation to assess for bruits or hums
- Neurologic examination to look for focal deficits
- Audiological examination for all patients presenting with tinnitus
- Imaging (CT/MRI) is recommended for patients with 1 or more of the following:**
 - Unilateral tinnitus
 - Asymmetric tinnitus
 - pulsatile tinnitus, and/or focal neurological deficits
- Routine blood test:** if a treatable cause of tinnitus is suspected: CBC (Anemia), TSH (hypothyroidism)
- Infectious workup:** FTA-ABS for syphilis
- Autoimmune workup:** ANA, ESR, rheumatoid factor) if suspected

**TREATMENT OF TINNITUS**

- After symptom onset, treatment should be started as early as possible to prevent the condition from becoming chronic.
- Treat any underlying conditions.
- Supportive treatment:** counseling, stress reduction, cognitive behavioral therapy, sound therapy etc...

↳ **Stress Reduction:** This includes using biofeedback, Deep breathing exercises, Relaxation to music etc...

↳ **Cognitive behavioral Therapy:** The more the patient understands what tinnitus is and is not the less negative effect. Once the patient fully cognizes - understands that tinnitus is similar to itching, the symptoms are reduced.

↳ **Masking:** When the body hears the same sound from the cell phone or sound device, this reduces the symptoms. There are various forms of masking. Essentially these masking sounds take the attention away from the internal tinnitus sound and replace it with relaxing sounds.

↳ Introduction of the same sound

↳ Introduction of an altered sound

↳ Music with the tinnitus sound removed

↳ White noise or pleasant sounds

↳ **Sleep improvement:** Tinnitus can affect normal sleep and therapy should be directed to better sleep hygiene.

- Tab. Alprazolam 0.5mg** (Alp, Xanax)
OR **Tab. Diazepam 5mg** (Valium)
OR **Tab. Clonazepam 0.5mg** (Revotril, Naze)
0 - 0 - 1 (HS)

- Softgel. Cod liver oil** (Seven seas, Seamega)
0 - 0 - 1 (OD)

Anti-depressants may be indicated for patients who do not respond to protocol therapy

- Tab. Amitriptyline 25mg** (Sensival) x HS titrated the dose if not respond. (Maximum dose: 25mg-150mg/day)
OR **Cap. Fluoxetine 20mg** (Depex, Flux) x OD after breakfast



VERTIGO

Definition: Vertigo is the sensation of spinning or swaying of oneself (internal vertigo) or of one's surroundings (external vertigo) while stationary.

Vertigo are divided into:

1. **Peripheral vertigo:** Involve vestibular end organs and their 1st order neurons (i.e. the vestibular nerve).
 - » The cause lies in the internal ear or the 8th nerve.
 - » They are responsible for 85% of all cases of vertigo.
2. **Central vertigo:** Involve central nervous system after the entrance of vestibular nerve in the brainstem and involve vestibulo-ocular, vestibulospinal and other central nervous system pathways

DIFFERENTIATING PERIPHERAL VERTIGO FROM CENTRAL VERTIGO

Characteristics	Peripheral vertigo	Central vertigo
Etiology	» Ménière's disease (endolymphatic hydrops) » Benign paroxysmal positional vertigo (semicircular canal debris) » Vestibular neuronitis » Labyrinthitis » Vestibulotoxic drugs » Head trauma » Perilymph fistula » Syphilis » Acoustic neuroma	» Vertebrobasilar insufficiency » Posterior inferior cerebellar artery syndrome » Basilar migraine » Demyelination (multiple sclerosis) » Brainstem ischemia (vestibular nuclei stroke) » Tumours of brainstem and fourth ventricle » Epilepsy » Cervical vertigo
Location of the underlying disorder	» Lesions of Inner ear: vestibulocochlear nerve, semicircular canals	» Lesions of CNS (cerebellum, brainstem)
HINTS Exam (HINTS = Head Impulse, Nystagmus, and Test of Skew)	» Head impulse test: usually abnormal in vestibular neuritis » Nystagmus » Typically horizontal Vertical or torsional nystagmus may be seen or elicited in BPPV » Direction of nystagmus does not change with gaze change. » Gaze fixation improves nystagmus » Skew deviation: absent	» Head impulse test: normal » Nystagmus » May be torsional, horizontal, or vertical » Direction of nystagmus changes with gaze change. » Gaze fixation does not reduce nystagmus » Skew deviation: present
Associated cerebellar symptoms (e.g., ataxia, dysmetria)	» Absent or mild	» Marked
Sense of motion	» Severe	» Mild
Associated hearing loss and/or tinnitus	» Common (e.g., Ménière disease, labyrinthitis)	» Rare
Associated focal neurological findings (e.g., diplopia)	» Rare	» Common

△ Vertigo
C/C:

Diagnostics

- » Diagnosis is clinical
- » Dix-Hallpike maneuver
- » supine head roll test

Rx

- » Vestibular rehabilitation therapy (Brandt-Daroff exercise, Cawthorne-Cooksey exercise), training on maintaining balance based on visual and proprioceptive clues
 - » Lifestyle recommendations: avoiding caffeine, salt and alcohol, avoiding triggers
 - » Canalith repositioning procedure: Epley maneuver
1. Tab. Betahistine 8mg, 16mg or 24mg (Serc, Enier, Setspin) x 8mg to 48mg x TDS/BD
OR Tab. Prochlorperazine 5mg (Stemetil) x TDS, increasing up to 30mg if not respond
OR Tab. Dimenhydrinate 50mg (Gravinate) x TDS (maximum dose 400mg/day)
 2. Tab. Alprazolam 0.5mg (Alp, Xanax)
OR Tab. Diazepam 5mg (Valium)
OR Tab. Clonazepam 0.5mg (Revotril, Naze)
0-0-1 (HS)

BENIGN PAROXYSMAL POSITIONAL VERTIGO (BPPV)

- Definition: Episodic vertigo triggered by certain changes in the position of the head
- Prevalence
 - BPPV is the most common type of peripheral vestibular vertigo with a prevalence of ~ 2%.
 - BPPV is the underlying cause in approx. 40% of geriatric patients presenting with dizziness.
- Sex: female > male
- Age: peak incidence between 50–60 years
- Clinical features:
 - » Episodic vertigo (spinning sensation)
 - Sudden ("paroxysmal") and recurrent episodes
 - Lasts several seconds (typically ≤ 1 min)
 - Triggered by certain head movements (positional vertigo) after a latency of a few seconds.
 - **Associated with:** Nystagmus, Risk of falls and subsequent injury, Nausea and vomiting
 - » Triggers: Quick rotation of the head relative to gravity is the main trigger of BPPV
 - Lying down, reclining, or standing up quickly
 - Rolling over in bed
 - Bending forwards
 - Suddenly jerking the head to look up or down

Diagnostic approach

Clinical diagnosis

Dix-Hallpike maneuver

- » The Dix-Hallpike maneuver should be performed in all patients with suspected BPPV to identify posterior canal BPPV
- » If the Dix-Hallpike maneuver is negative, the supine head roll test should be performed to assess for lateral canal BPPV

» Indication

- First-line test for suspected BPPV
- Gold standard test to diagnose suspected posterior semicircular canal BPPV
- Suspected anterior semicircular canal BPPV

» Characteristic findings

- **Positive Dix-Hallpike test:** positional vertigo and nystagmus triggered during the maneuver
- **Direction of nystagmus**
 - Posterior canal BPPV: upbeat nystagmus with ipsiversive torsional nystagmus component
 - Anterior canal BPPV: downbeat nystagmus with ipsiversive torsional nystagmus

Procedure of Dix-Hallpike maneuver

1. Ask the patient to sit upright on the examination bed and to keep their eyes open during the procedure.
2. Rotate the head by 45° towards the affected side.
3. Keeping the neck rotated, quickly lay the patient in a supine position with the neck slightly extended (approx. 20°) and the affected ear held down at 45°.
4. Hold this position for 20–30 seconds.
 - Examine the eyes for nystagmus; if present note latency, direction, and duration of nystagmus
 - Inquire if the patient is experiencing vertigo
 - Wait for resolution of nystagmus and vertigo
5. Slowly reposition the patient into an upright posture with neck in neutral position and observe for reversal of nystagmus.
6. If negative (that is, no nystagmus/vertigo), repeat the maneuver with the head turned to the unaffected side in step-2

Supine Head Roll Test

» Characteristic findings

- Positional vertigo and nystagmus triggered during the maneuver
- **Direction of nystagmus in lateral canal BPPV:**
 - Bilateral horizontal nystagmus with eyes beating toward the ground (geotropic nystagmus)
 - Bilateral horizontal nystagmus with eyes beating toward the ceiling (apogeotropic nystagmus)

» Procedure of supine head roll test

1. Ask the patient to lie in a supine position and to keep their eyes open during the procedure.
2. Position the patient's head in neutral position.
3. Quickly turn the patient's head by 90° to one side and examine for nystagmus.
4. Wait for nystagmus to subside.
5. Reposition the patient's head to neutral position, reassess for nystagmus; allow nystagmus to subside.
6. Repeat steps on the opposite side.



Rx

TREATMENT OF BENIGN PAROXYSMAL POSITIONAL VERTIGO (BPPV)

- Vestibular rehabilitation therapy (Brandt-Daroff exercise, Cawthorne-Cooksey exercise), training on maintaining balance based on visual and proprioceptive clues
- Lifestyle recommendations: avoiding caffeine, salt and alcohol, avoiding triggers
- Canalith repositioning procedure: Epley maneuver

1. Tab. Betahistine 8mg, 16mg or 24mg (Serc, Enier, Setspin)

8mg or 16mg = 1-1-1 (TDS), 24mg = 1-0-1 (BD)

OR Tab. Prochlorperazine 5mg (Stemetil) x 1-1-1 (TDS) titrated up to 30mg if not respond.

OR Tab. Cinnarizine (Tab. Stugeron 25mg OR Cap. Stugeron 75mg)

Tablets = 1-1-1 (TDS) or Capsules = OD/BD per day

OR Tab. Dimenhydrinate 50mg (Gravinate) x 1-1-1 (TDS) Maximum Dose: <400mg/day

2. Tab. Alprazolam 0.5mg (Alp, Xanax, Praz)

OR Tab. Diazepam 5mg (Valium)

OR Tab. Clonazepam 0.5mg (Revotril, Naze)

0-0-1 (HS)

• Surgical treatment

» Indication

- Intractable BPPV
- Severe and frequent recurrences

» Options

- Singular neurectomy
- Posterior semicircular canal occlusion

Canalith Repositioning Maneuvers (CRM)

• **Definition:** Set of specific sequential maneuvers performed to mobilize the otoconia out of the involved semicircular canal and back into the vestibule

• **Indication:** first-line treatment for BPPV

• **General Considerations**

- » CRM can be performed immediately after identifying the affected canal on a provoking maneuver.
- » A trained general practitioner can perform the Dix-Hallpike maneuver and Epley maneuver. ENT referral is recommended in patients with persistent or recurrent symptoms.
- » Potential side effects include nausea, vomiting, and postural instability lasting for approximately 24 hrs.
- » Antiemetics or vestibular suppressants may be giving prophylactically before performing CRM.
- » Patients with frequent recurrences can be taught to perform these maneuvers themselves at home.

• **Outcome**

- » Up to 80-90% success rate, patients will be cured by a single manoeuvre.
- » Recurrences requiring repeat CRM are expected.
- » Canal conversion

Procedure of Epley Maneuver

1. The initial steps are the same as those of the Dix-Hallpike maneuver
 - » Ask the patient to sit upright on the examination table and to keep their eyes open during the procedure.
 - » Rotate the head by 45° towards the affected side.
 - » Keeping the neck rotated, quickly lay the patient in a supine position with the neck slightly extended (approx. 20°) & the affected ear facing down at 45°
2. Hold this position for 30 seconds or until the resolution of nystagmus.
3. Turn the patient's head by 90° toward the unaffected side; hold this position for 30 seconds or until resolution of nystagmus
4. Turn the patient's head and body by 90° towards the unaffected side such that the patient is now lying on their side with their face turned toward the ground.
5. Hold this position for 30 seconds or until the resolution of nystagmus.
6. Bring the patient back to a seated, upright position with the head in the neutral position.
7. After completion of the maneuver, ask the patient to remain in this position for about 15 minutes.



EAR, NOSE AND THROAT DRUG BRANDS IN PAKISTAN

ANTI-ALLERGIC/ANTIHISTAMINE DRUGS

Pheniramine malate	» Tab. Avil 25mg, Tab. Avil 50mg » Inj. Avil 50mg/2ml » Inj. Zafvil 50mg/2ml » Syp. Avil 15mg/5ml
Hydroxyzine	» Tab. Atarax 10mg, Tab. Atarax 25mg » Tab. Roxyzin 10mg, Tab. Roxyzin 25mg
Promethazine	» Syp. Phenergan » Tab. Avomine 25mg
Dimenhydrinate	» Tab. Gravinate 50mg » Syp. Gravinate 12.5mg » Inj. Gravinate 50mg/1ml
Chlorpromazine	» Tab. Largactil 10mg, 25mg
Prochlorperazine	» Tab. Stemetil 5mg
Cinnarizine	» Tab. Stugeron 25mg » Cap. Stugeron 75mg
Betahistine	» Tab. Serc 8mg, 16mg and 24mg » Tab. Enier 8mg, 16mg and 24mg » Tab. Setspin 8mg, 16mg and 24mg
Cetirizine	» Tab. Rigix 10mg, Syp. Rigix 5mg/5ml » Rigix drops 10mg/ml » Tab. Zyrtec 10mg, Syp. Zyrtec 5mg/5ml » Tab. Baydal 10mg, Syp. Baydal 5mg/5ml
Levocetirizine	» Tab. Belair 5mg, Tab. Xyzal 5mg » Tab. Atiza 5mg, Syp. Atiza 2.5mg/5ml » Tab. T-day 5mg, Syp. T-day 2.5mg/5ml » Tab. Neo-Sedil 5mg, Syp. Neo-Sedil 2.5mg/5ml
Ebastine	» Tab. Kestine 10mg, 20mg, Syp. Kestine 5mg » Tab. Beceptor 10mg and 20mg » Tab. Ebak 10mg and 20mg
Loratadine	» Tab. Lorin NSA 10mg, Syp. Lorin NSA 5mg/5ml » Tab. Softin 10mg, Syp. Softin 5mg/5ml » Tab. Loril 10mg, Syp. Loril 5mg/5ml » Tab. Xylor 10mg, Syp. Xylor 5mg/5ml
Tab. Loratidine 10mg + Pseudoephedrine 120mg	» Tab. Softin-P » Tab. Rhilor-D
Desloratadine	» Tab. Destina 5mg, Tab. Larinex 5mg, Tab. Softin OD » Tab. Desora 5mg, Tab. Desora 0.5mg/ml » Tab. Neo-Antial 5mg, Syp. Neo-Antial 0.5mg/ml » Tab. Jordin-D 5mg, Syp. Jordin-D 0.5mg/ml
Fexofenadine	» Tab. Telfast 60mg, 120mg and 180mg » Tab. Fexo 60mg, 120mg and 180mg » Tab. Softin-F 60mg, 120mg and 180mg » Tab. Fexet 60mg, 120mg and 180mg
Fexofenadine 60mg + Pseudoephedrine 120mg	» Tab. Telfast-D » Tab. Fexet-D » Tab. Fexo-D



INTRA-NASAL DROPS/ SPRAYS

Sodium chloride 0.9%	» Normal saline 0.9% Nasal sprays » Norsaline-P Nasal spray/drops » Salinase Nasal drops
Na Cromoglycate 2% + Xylometazoline 0.025%	» Oxycrom
Sodium Cromoglycate 4%	» Oxycrom-P
Ephedrine 5mg/ml + Fluprednisolone 0.025mg/ml + Naphzoline 1.25mg/ml	» Rhinosone nasal sprays
Xylometazoline 0.1%	» Xynosine nasal sprays » Xolisan nasal sprays » Nasomet nasal spray
Xylometazoline 0.05%	» Otrivin nasal drops for children » Xynosine nasal drops for children
Beclometasone	» Rinoclenil nasal sprays
Triamcinolone acetonide	» Nasacort AQ Nasal Spray (55mcg/dose) » Nasarin Nasal Spray (55mcg/dose)
Fluticasone propionate 0.05%	» Flixonase nasal sprays » Flexosone nasal sprays » Ticovate nasal sprays » Avamys nasal sprays
Mometasone Furate 0.05%	» Hivate nasal sprays » Rinelon nasal sprays
Azelastine Hydrochloride 0.1%	» Azosin
Flunisolide 0.025%	» Tarisin nasal spray

EAR DROPS

Polymyxin + Lidocaine	» Otocain Ear drops
Chloramphenicol 0.1%	» Remicol Ear drops » Mexclor Ear drops
Tobramycin	» Ototob Ear drops
Tobramycin + Dexamethasone	» Tobec-D Ear drops » Dexatob Ear drops » Vegatob Ear drops



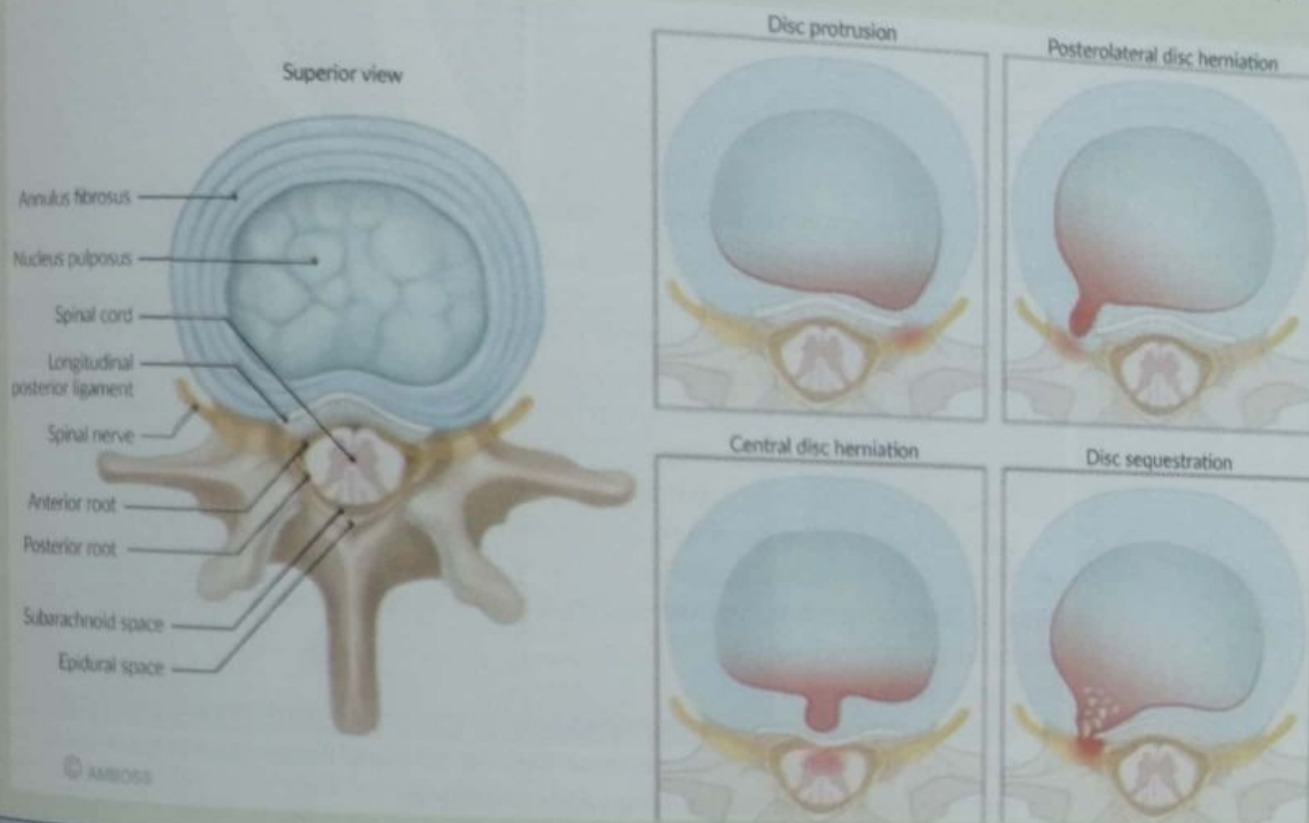
Gentamicin	» Gentycin Ear drops » Otogen Ear drops
Gentamicin + Hydrocortisone	» Gentycin HC Ear drops
Ofloxacin	» Otoflox 0.3% Ear drops » Otoflox 0.6% Ear drop » Oflocin 0.3% Ear drops » Oflocin 0.6% Ear drops » Kunoxy 0.3% Ear drops » Kunoxy 0.6% Ear drops
Ciprofloxacin	» Cipotic Ear drops » Prolotic Ear drops
Ciprofloxacin + Dexamethasone	» Cipotic-D Ear drops » Dexcip Ear drops » Zeprodex Ear drops » Quinodex Ear drops
Ciprofloxacin + Hydrocortisone	» Hipro HC Ear drops
Ciprofloxacin + Lidocaine	» Cipocain Ear drops » Lignocip Ear drops » Zeprocaine Ear drops
Dexamethasone + Framycetin	» Fradex Ear and Eye drops
Polymyxin + Hydrocortisone + Neomycin	» Otosporin ear drops
Polymyxin + Lidocaine + Propylene Glycol	» Lidosporin Ear drops
Betamethasone	» Betnesol Ear, eye and nose drops
Betamethasone + Neomycin	» Probeta-N Ear & eye drops » Betnesol-N Ear, eye and nose drops
Triamcinolone + Neomycin + Gramicidin + Nystatin	» Xecomb Ear drops



APPROACH TO DEGENERATIVE DISK DISEASES

Degenerative disk disease refers to a group of conditions in which disk material is displaced into the spinal canal. The condition can be asymptomatic or manifest as radiculopathy (due to compression of a spinal nerve root) or myelopathy (due to compression of the spinal cord). The site of nerve or cord compression can often be determined based on the patient's neurological deficits.

- **Disk protrusion:** protrusion of the vertebral disk nucleus pulposus through the annulus fibrosus
- **Disk prolapse (disk extrusion or disk herniation):** complete extrusion of the nucleus pulposus through a tear in the annulus fibrosus
- **Disk sequestration:** extrusion of the nucleus pulposus and separation of a fragment of the disk
- **Spondylosis:** a broad term used to describe degenerative changes of the spine that may result in irritation and/or damage of the adjacent nerve roots or spinal cord



Pathophysiology

- **Intervertebral disk consists** of a dense outer ring (**annulus fibrosus**) & a gelatinous core (**nucleus pulposus**)
- These structures work together as a shock absorber by distributing high axial pressure evenly onto the cover plates and base units of the vertebral bodies.
- High pressure on the vertebral disks leads to fluid loss, and as a result, body height decreases physiologically by 1-2 cm during the day.
- **Compression, tension, shear, and torque stresses on the spinal disk** → degenerative changes (e.g., dehydration, annular tear) → disk protrusion or herniation through the annulus fibrosus into the central canal → adjacent nerve root impingement → sensorimotor deficits in affected nerve root
- **Posterolateral disk herniation/protrusion (common)** → compression of the transversing nerve root → compressive radiculopathy
- **Central disk herniation/protrusion (less common)** → compression of the spinal cord (above L1 - L2) or cauda equina (below L2) → compressive myelopathy

Clinical features

- Degenerative disk disease may be asymptomatic
- It may be detected incidentally on radiology performed for an unrelated condition.
- Examination findings vary depending on the location and severity of nerve root compression.
- **Acute onset of severe neck or back pain**
 - **Radicular pain:** pain that radiates to the legs (sciatic pain) or arms
 - The pain is either stabbing in nature or resembles an electric shock.
 - Pain in...



- » Pain decreases with minor changes in position (e.g., taking a short walk).
- » **Features of radiculopathy:** lower motor neuron signs of the affected nerve root (typically unilateral)
 - » Paresthesia of the affected dermatome
 - » Muscle weakness and atrophy of the related myotome
 - » Absent or diminished deep tendon reflexes
- » **Features of myelopathy or cauda equina syndrome** (typically bilateral)
 - » Paresthesia below the level of compression
 - » **Motor deficits**
 - At the level of compression: lower motor neuron signs
 - Below the level of compression
 - Upper motor neuron signs in spinal cord compression and conus medullaris syndrome
 - Lower motor neuron signs in cauda equina syndrome
- » May be associated with gait disturbances, bladder dysfunction, and/or bowel dysfunction

Red flags features for back pain (acute)

Character	Features
» Patient characteristics	» Age < 18 or > 50 years » Immunosuppression
» Relevant medical history	» History of cancer or unexplained weight loss » History of abdominal aortic aneurysm » Recent history of any of the following: Bacterial infection, Spinal anesthesia, Spinal surgery and Significant trauma related to age
» Medication use	» Long-term steroids, Anticoagulants or Intravenous drugs
» Pain characteristics	» Pain that does not improve with rest and/or worsens at night » Persistent or progressive pain &/or neurological findings despite > 4 weeks conservative therapy
» Examination findings	» Fever, Abnormal vitals (Hypertension, hypotension, and/or tachycardia, bradycardia) » Signs of aortic pathology, including: ▪ Pulse deficits in the lower extremities ▪ Unequal blood pressure measurements in the upper extremities ▪ The murmur of aortic regurgitation » Signs of cord compression syndromes (spinal cord compression, cauda equina syndrome, conus medullaris syndrome), such as: ▪ Motor weakness ▪ Spasticity and hyperreflexia (upper motor neuron signs) distal to the site of compression ▪ Flaccid paralysis & hyporeflexia can occur distal to the site of compression in spinal shock ▪ Paresthesias or anesthesia (including saddle anesthesia) ▪ Bladder, bowel, or sexual dysfunction

Management and evaluation of degenerative disk diseases

Focused history and clinical examination: Assess for red flag features of acute back pain in all patients. A thorough neurological exam is essential to adequately triage patients who need urgent imaging and neurosurgery consult.

- » Examine sensation, power (motor strength), deep tendon reflexes, and superficial reflexes (e.g., Babinski reflex) below the level of the pain bilaterally.
- » Assess for signs of nerve root irritation (e.g., straight leg raise test).
- » Assess perianal sensation and anal tone.

MRI spine plain (without IV contrast): MRI Cervical spine or MRI Lumbar spine

- » Best initial investigation for suspected radiculopathy, myelopathy, or cauda equina syndrome

» **Supportive findings**

- » **Disk degeneration:** Sclerosed, dehydrated disk that appears hypointense on T2-weighted images
- » **Disk prolapse/disk herniation:** herniation of disk tissue with surrounding edema
- » Evidence of impingement/compression of a spinal nerve or the spinal cord may be visible, e.g.:
 - Focal narrowing of the spinal canal
 - Compression of the thecal sac
 - Edema of the spinal cord (appears hyperintense on T2-weighted images)

X-ray spine

- » Consider for patient with new or increasing non-traumatic cervical pain who do not have red flag features.
- » Flexion-extension views are useful for identifying spondylolisthesis and spinal instability.
- » **Findings (on A.P & lateral views):** Disk space narrowing, vertebral body osteophytes, endplate & facet sclerosis



MRI ANATOMY OF THE CERVICAL SPINE & LUMBER SPINE



Figure A- Lumber Spine MRI (T2 weighted) Anatomy

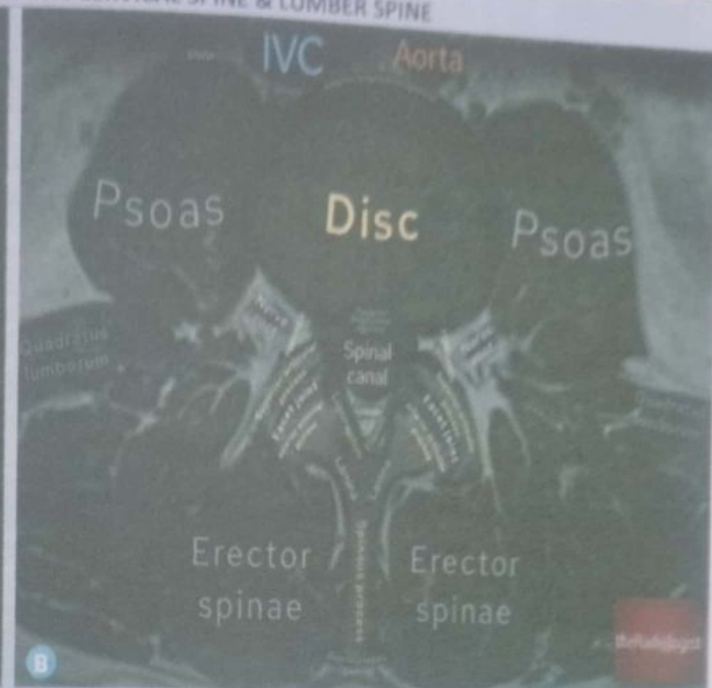


Figure B- Axial Lumber Spine MRI (T1 weighted) Anatomy

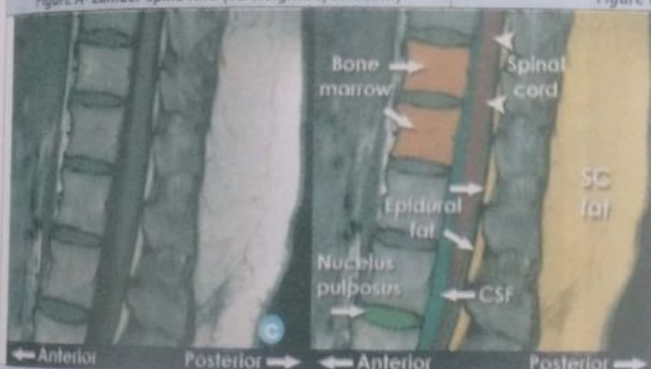


Figure C- Normal Anatomy of the spine - MRI lumbar spine (without contrast)



Figure D- MRI lumbar spine plain (T2-weighted; sagittal plane)

Findings: Spinal disk herniation with migration → The desiccated disk at L4-5 is hypointense and the disk space is narrowed. Extruded disk material (green overlay) has migrated to the level of the L5 vertebral body and is compressing the thecal sac.



Figure E- Lumber Spine MRI (T2 weighted) Anatomy

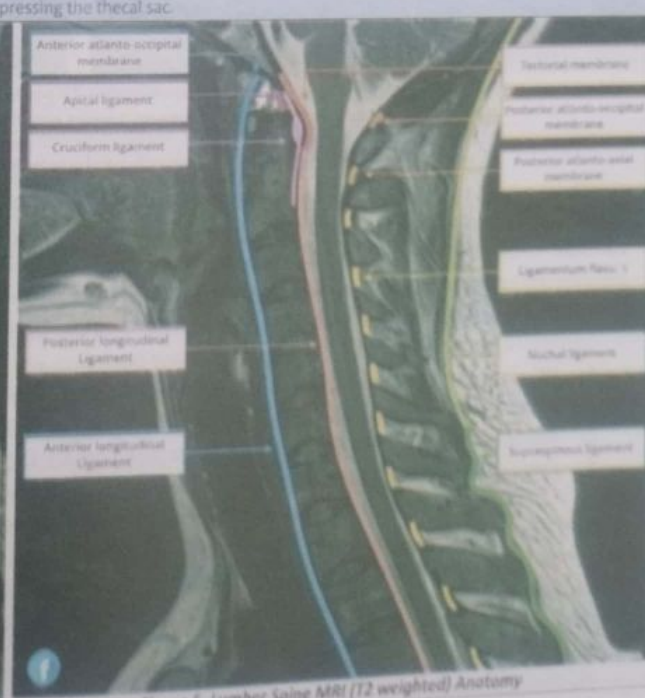


Figure F- Lumber Spine MRI (T2 weighted) Anatomy





MRI lumbar spine T (Figure: G- T1-weighted axial view and Figure: H- T2-weighted sagittal view)
 Spinal disk herniation: Disk herniation between L5 and S1 (right side, red) with narrowing of the spinal canal (see axial view). In the T1-weighting, epidural fat tissue appears hyperintense (green) and cerebrospinal fluid (CSF) hypointense; in the T2-weighting, CSF is hyperintense.



Figure: I- MRI cervical spine (T2-weighted; sagittal plane)
 Cervical disk herniation at C6-C7 (green overlay) produces a prominent anterior extradural impression with spinal canal narrowing and cord compression.

Treatment approach of degenerative disk diseases

- Identify and treat compressive spinal emergencies immediately, if present.
- Urgent MRI is typically not required; Considerer MRI if symptoms do not improve within 6 weeks.
- Consider referral to neurosurgery to assess whether surgery is required for persistent symptoms.
- Educate the patient on symptoms of compressive spinal emergencies, if develop urgent specialist checkup
- Initiate Conservative management (Explained below "See low back pain, Cervical or lumbosacral Radiculopathy")**
 - » Treatment is similar to that for non-specific lower back pain and neck pain (Explained below).
 - 1. **Physiotherapy with exercises to strengthen the back and neck**
 - 2. **Continuation of daily activities** (minimize bed rest)
 - 3. **Analgesia with NSAIDs:** Paracetamol, Naproxen sodium, Diclofenac sodium, Lornoxicam, Piroxicam etc.
 - 4. **Consider muscle relaxants** (Tiznadine, Thiocolchicoside) **and short-term opioid analgesic** (Tramadol, Tapentadol)
 - 5. Consider a short course of oral corticosteroids (Prednisolone) for pain related to radiculopathy.
 - » Advise patients that symptom improvement is typically gradual (up to several weeks).
 - » **For patients with severe pain, consider peri-radicular therapy:** image-guided injection of local anesthetic (Ropivacaine) and corticosteroids at the intervertebral foramen to reduce inflammation and edema at the affected nerve root.
- Surgical procedure:** Discectomy and Laminectomy
 - » **Urgent:** significant or progressive neurological deficits, bowel or bladder incontinence, compressive spinal emergencies
 - » **Elective:** persistent or progressive radiculopathy despite conservative management



CERVICAL RADICULOPATHY (BRACHIALGIA/PINCHED NERVE)

Clinical features

Symptoms

- » Neck pain commonly associated with radiculopathy
- » Can manifest with difficulty with fine motor skills
- » Can be accompanied by headache and/or shoulder pain

» **Examination findings:** May be normal or show specific motor or sensory deficits depending on the nerve root affected (mention in below table)

1. Overview of cervical radiculopathies

Radiculopathy	Nrv root involve	Sensory deficits	Motor deficits	Reduction of reflexes
» C3/C4 radiculopathy	C2-C4	▪ Shoulder and neck area	▪ Scapular winging	▪ None
» C5 radiculopathy	C4-C5	▪ Anterior shoulder	▪ Biceps and deltoid	▪ Biceps reflex
» C6 radiculopathy	C5-C6	▪ From the upper lateral elbow over the radial forearm up to the thumb and radial side of index finger	▪ Biceps and wrist extensors	▪ Biceps reflex ▪ Brachioradialis reflex
» C7 radiculopathy	C6-C7	▪ Palmar: fingers II-IV (II ulnar half, III entirely, IV radial half) ▪ Dorsal: medial forearm up to fingers II-IV	▪ Triceps, wrist flexors, and finger extensors	▪ Triceps reflex
» C8 radiculopathy	C7-T1	▪ Fingers IV (ulnar half) and V, hypothenar eminence, & ulnar aspect of the distal forearm	▪ Finger flexors	▪ None

2. Provocative maneuvers

- **Hoffmann reflex:** A positive result suggests cervical myelopathy.
- **Neck compression test (Spurling maneuver):** screens for cervical radiculopathy
 - ↳ Tilt and rotate the neck toward the affected side while applying downward pressure (axial loading) to the head
 - ↳ The test is positive if it produces pain and/or paresthesia that radiates to the motor or sensory area of the affected nerve root.

△ Cervical Radiculopathy C/C:

Clinical presentation

"See features of degenerative disc diseases"

- » Pain in the neck, shoulder blade or arm.
- » Numbness
- » Tingling or the feeling of "pins and needles" in the fingers or hand
- » Weakness in the muscles of the arm, shoulder, or hand
- » Loss of sensation

Diagnosis and investigation

"See degenerative disc diseases"

- » X-Ray neck lateral view
- » MRI cervical spine
- » Vitamin-D level

Rx

1. Cap. Gabapentin 100mg OR 300mg (Gabix, Neogab)
OR Cap. Pregablin 50mg OR 75mg OR 100mg (Gabica, Zeegap, Syngab)
I - 0 - I (BD)
2. Tab. Paracetamol + Orphenadrine citrate (Neubrol forte, Provas-N)
OR Tab. Paracetamol + Tramadol (Tonoflex-P, Distalgesic)
I - I - I (TDS)
OR Tab. Diclofenac sodium 50mg OR 100mg (Voren, Voltral)
OR Tab. Naproxen sodium 500mg (Flexin, Neoprox, Synflex)
I - 0 - I (BD)
3. Tab. Methylcobalamin 500mcg (Methycobal, Cobalamin)
I - 0 - I (BD)
4. Cap. Esomeprazole 40mg (Nexum, Esso)
OR Cap. Omeprazole 40mg (Risek, Ruling)
I - 0 - 0 (OD)
کہاں سے 30 منٹ پہلے
5. ± **Muscle Relaxants:** To alleviate muscle spasms.
↳ Tab. Tizanidine 2mg OR 4mg (Movax, Ternalin)
I - 0 - I (BD)



LUMBOSACRAL RADICULOPATHY

Clinical features

Symptoms

- » Low back pain (lumbago) commonly associated with radiculopathy
- » Pain characteristically worsens with lumbar flexion (e.g., on sitting).

Examination findings: May be normal or show specific motor or sensory deficits depending on the nerve root affected (mention in below table)

- ❖ Worsening of low back pain with lumbar flexion (e.g., on sitting) is suggestive of lumbar disk herniation, while improvement of pain with lumbar flexion is suggestive of lumbar spinal stenosis.
- ❖ Back pain associated with bowel or bladder dysfunction is concerning for spinal cord compression, cauda equina syndrome, and conus medullaris syndrome.

1. Overview of lumbosacral radiculopathies

Radiculopathy	N. Root involve	Sensory deficits	Motor deficits	Reduction of reflexes
L3 radiculopathy	L2-L4	Anterolateral area of the thigh	Hip flexion Knee extension Hip adduction	Adductor reflex Patellar reflex
L4 radiculopathy	L3-L4	Anterolateral thigh, area over the patella, medial aspect of the leg, medial malleolus	Knee extension Hip adduction	Patellar reflex
L5 radiculopathy	L4-L5	Lateral aspect of the thigh & knee, anterolateral aspect of the leg, dorsum of the foot, & the big toe	Tibialis ant. muscle (foot dorsiflexion): difficulty heel walking (foot drop) Extensor hallucis longus muscle (first toe dorsiflexion)	Posterior tibial reflex (medial hamstring)
S1 radiculopathy	L5-S1	Dorsolateral aspect of thigh and leg, and the lateral aspect of the foot	Peroneus longus & brevis muscle (foot eversion) & gastrocnemius muscle (foot plantarflexion): difficulty toe walking	Achilles reflex Lateral hamstring reflex
S2 radiculopathy	S1-S4	Post. aspect of the thigh and leg	None	Bulbocavernosus reflex
S3 radiculopathy		(S2), perineum (S3-S4), perianal		Perineal reflex
S4 radiculopathy		(S4)		

2. Provocative maneuvers: Leg raising maneuvers are used to screen for lumbosacral radiculopathy

- **Straight leg raise test (Lasegue sign):** A straight leg raise leads to increased pain in the ipsilateral leg with radiation to the motor or sensory area of the affected nerve root.
- **Bragard sign:** A straight leg raise leads to increased pain in the ipsilateral leg; lowering the leg to just below the level where pain is produced and pulling the foot to dorsiflexion reproduces the pain.
- **Crossed straight leg raise test:** A crossed straight leg raise leads to pain in the ipsilateral leg radiating to the motor and sensory area of the affected nerve root.
- **Reverse straight leg raise test:** A reverse straight leg raise leads to pain in the ipsilateral leg radiating to the motor and sensory area of the affected nerve root.

△ Lumbosacral Radiculopathy

C/C:

Clinical presentation

"See features of degenerative disc diseases"

- » Numbness and tingling sensation in your arms, hands, leg, and foot
- » Pain radiates to buttocks and lower extremities
- » Pain or feeling of cramps in legs after standing for a long period of time or while walking.
- » Pain relieved by sitting or lying down and increase by standing or walking.

Diagnosis and investigation

"See degenerative disc diseases"

- » X-Ray lumbosacral
- » MRI lumbosacral spine
- » Vitamin-D level

Rx

Conservative treatment of lumbosacral radiculopathy is similar to low back pain

1. Cap. Pregablin 50mg OR 75mg OR 100mg (Gabica, Zeegap)
1-0-1 (BD)
2. Tab. Paracetamol + Orphenadrine citrate (Neubrol forte)
1-1-1 (TDS)
OR Tab. Naproxen sodium 500mg (Flexin, Neoprox)
1-0-1 (BD)
3. Tab. Methylcobalamin 500mcg (Methycobal, Cobalamin)
1-0-1 (BD)
4. Cap. Esomeprazole 40mg (Nexum, Esso)
1-0-0 (OD) x (30 دن تک)



LOW BACK PAIN

- Definition: Pain and/or stiffness localized to the lower back (below the costal margin) and above the buttocks. May be accompanied by pain radiating down the legs.
- Associated factors: Poor posture, sedentary lifestyle, low physical activity, Activities involving heavy lifting, increasing age and psychological stressors (e.g., stress, anxiety, depression)

Etiology

1. Mechanical (80-90%): trauma (e.g., spinal fracture)
2. Unknown cause: attributed to muscle tension or ligament injury (65-70%)
3. Anatomical: scoliosis, kyphosis, transitional vertebra
4. Degenerative: disc herniation, spinal stenosis, disc protrusion, spondylolisthesis, spondylosis
5. Syndromes due to surgery failure on the spine: arachnoiditis, epidural adherence, recurrent hernia
6. Inflammatory: ankylosing spondylitis, reactive arthritis, rheumatoid arthritis, inflammatory bowel diseases
7. Infectious: abscess (e.g., paraspinal, epidural), osteomyelitis, discitis
8. Malignant: metastases, tumors, multiple myeloma
9. Others: Instability, Osteophyte injury of nerve root, Paget disease, osteoporosis and somatoform disorder

Classification

- According to severity
 - » Uncomplicated: without red flag features for acute back pain
 - » Complicated: with red flag features for acute back pain
 - » See "Red flag features for acute back pain." (mention above in degenerative disc diseases)
- According to duration
 - » Acute low back pain: up to 4-6 weeks
 - » Subacute low back pain: 6-12 weeks
 - » Chronic low back pain: > 12 weeks

Diagnostic Workup

- Laboratory test
 - » CBC & inflammatory markers (ESR, CRP): for suspected spinal infections, inflammatory arthritis, or malignancy
 - » Serum calcium and vitamin D levels: for suspected fragility fractures
 - » Rheumatoid factor and HLA-B27: for suspected inflammatory arthritis
 - » Blood cultures: for suspected spinal infections
- MRI lumbosacral spine plain (without IV contrast): Disk degeneration, dehydrated disk, disk prolapse/herniation, compression of a spinal nerve, focal narrowing of the spinal canal, and compression of the thecal sac.
- X-ray spine (A.P & lateral views): Disk space narrowing, vertebral body osteophytes, endplate & facet sclerosis

Approach to the management

- Identify and treat compressive spinal emergencies immediately, if present.
- Focused history and clinical examination
- Urgent MRI is typically not required; Considerer MRI if symptoms do not improve within 6 weeks.
- Consider referral to neurosurgery to assess whether surgery is required for persistent symptoms.
- Educate the patient on symptoms of compressive spinal emergencies, if develop urgent specialist checkup
- Initiate Conservative management
 - » Treatment is similar to that for non-specific lower back pain and neck pain (Explained below).
 - 1. Physiotherapy with exercises to strengthen the back and neck
 - 2. Continuation of daily activities (minimize bed rest)
 - 3. Analgesia with NSAIDs: Paracetamol, Naproxen sodium, Diclofenac sodium, Lornoxicam, Piroxicam etc.
 - 4. Consider muscle relaxants (Tiznadine, Thiocolchicoside) & short use opioid analgesic (Tramadol, Tapentadol)
 - 5. Consider a short course of oral steroids (Prednisolone, dexamethasone) for pain related to radiculopathy.
 - » Advise patients that symptom improvement is typically gradual (up to several weeks).
 - » For patients with severe pain, consider peri-radicular therapy: Image-guided injection of local anesthetic (Ropivacaine) & steroids at the intervertebral foramen to reduce inflammation & edema at the affected nerve root
- Surgical procedure: Discectomy and Laminectomy
 - » Urgent: significant or progressive CNS deficits, bowel or bladder incontinence, compressive spinal emergencies
 - » Elective: persistent or progressive radiculopathy despite conservative management



△ Low back pain
C/C:

- Numbness and tingling sensation in your arms, hands, leg, and foot
- Pain radiates to buttocks and lower extremities.
- Pain or feeling of cramps in the legs after standing for a long period of time or while walking.
- Pain relieved by sitting or lying down and increase by standing or walking.
- The pain usually goes away when the person either bends forward or sits down (Pain relieved by forward flexion)
- Pain exacerbated by standing and walking.

Rx

Low back pain prescription #1

(Neubrol forte, Provas-N)

1. Tab. Paracetamol + Orphenadrine citrate
OR Tab. Paracetamol + Tramadol (Tonoflex-P, Distalgasic)
1-1-1 (TDS)
2. Tab. Eperisone 50mg (Myonal, Perispa, SMUR)
1-0-1 (BD)
3. Tab. Vitamin-B complex (Neurobion, Becefol)
0-0-1 (OD)

Rx

Low back pain prescription #2

1. Cap. Pregablin 50mg OR 75mg OR 100mg (Gabica, Prelin)
OR Cap. Gabapentin 100mg OR 300mg (Neogab, Gabix)
1-0-1 (BD)
2. Tab. Naproxen sodium 500mg (Flexin, Neoprox, Synflex)
OR Tab. Diclofenac potassium 50mg (Cafam, Sofac-P, Maxit)
OR Tab. Diclofenac sodium 50mg OR 75mg (Voren, Voltral)
1-0-1 (BD)
3. Tab. Mecobalamin 500mcg (Methycobal, Cobalamin)
1-0-1 (BD)
4. Cap. Esomeprazole 40mg (Esso, Nexum)
OR Cap. Omeprazole 40mg (Ruling, Omezol, Risek)
1-0-0 (OD)
کھانے سے 30 منٹ پہلے

If pain is more severe than add opioid analgesic

5. Tab. Tramadol 100mg (Tramol SR, Tonoflex SR, Vexnil SR)
0-0-1 (OD), 1-0-1 (BD)

Rx

Low back pain prescription #3

1. Tab. Lacosamide 50mg OR 100mg OR 150mg (Lalap, Lecoles)
OR Cap. Pregablin 50mg OR 75mg OR 100mg (Gabica, Prelin)
1-0-1 (BD)
2. Tab. Naproxen sodium 500mg (Flexin, Neoprox, Synflex)
OR Diclofenac sodium 50mg OR 75mg (Voren, Voltral)
1-0-1 (BD)
3. Tab. Mecobalamin 500mcg (Methycobal, Cobalamin)
1-0-1 (BD)
4. Cap. Dexlansoprazole 30mg (Razodex, Dextop)
0-0-1 (OD)
کھانے سے 30 منٹ پہلے
5. Tab. Tizanidine 2mg OR 4mg (Movax, Musidin)
OR Cap. Thiocolchicoside 4mg (Muscoril, Thiolax)
1-0-1 (BD, 1-0-1 (OD)



SCIATICA PAIN

Clinical features

1. **Radiating Pain:** The pain usually starts in the lower back or buttock and radiates down the leg. It can extend all the way to the foot.
2. **Sharp/burning sensation:** The pain can be sharp, burning, or searing. It may feel like an electric shock.
3. **Unilateral Pain:** Typically, sciatica affects only one side of the body.
4. **Numbness or Tingling:** Some people experience numbness, tingling, or muscle weakness along the nerve pathway.
5. **Worsening with Movement:** Symptoms often worsen with prolonged sitting, standing, sneezing, or coughing.
6. **Difficulty Moving:** Severe cases may cause difficulty in moving the leg or foot.

Diagnostic workup

1. **Medical History and Physical Examination:** A doctor will review symptoms and medical history and perform a physical examination, focusing on the spine and legs.
2. **X-rays L/S spine:** To rule out fractures or bone abnormalities.
3. **MRI L/S spine:** To provide detailed images of soft tissues, including herniated discs and nerve compression.
4. **CT scan:** Sometimes used to provide detailed cross-sectional images.
5. **Electromyography (EMG):** To measure the electrical activity of muscles and nerves, which can help identify nerve damage.

How to Avoid Sciatic Pain

It may not be possible to prevent Sciatica, but these lifestyle changes may help:

- Avoid back strain -- lift things properly!
- Maintain your ideal weight
- Eat a healthy diet
- Exercise regularly
- Practice good posture
- Quit smoking



TREATMENT OF SCIATICA (Prescription #1)

1. **Rest and Activity Modification:** Short-term rest and avoiding activities that worsen the pain.
2. **Physical Therapy:** Exercises to strengthen the muscles supporting the spine, improve flexibility, and promote proper posture.
3. **Tab. Paracetamol + Orphenadrine citrate** (Neubrol forte, Provas-N)
OR **Tab. Paracetamol + Tramadol** (Tonoflex-P, Distalgesic)
I - I - I (TDS)
4. **Nerve pain (Neuropathic pain) medications:**
↳ **Cap. Gabapentin 100mg OR 300mg** (Neogab, Gabix)
↳ OR **Cap. Pregablin 50mg OR 75mg** (Gabica, Zeegab, Syngab)
I - 0 - I (BD)
5. **Tab. Mecobalamin 500mcg** (Methycobal, Cobalamin)
I - 0 - I (BD)
6. **± Muscle Relaxants:** To alleviate muscle spasms.
↳ **Tab. Tiznadine 2mg OR 4mg** (Movax, Ternalin)
I - 0 - I (BD) OR 0 - 0 - I (OD)



TREATMENT OF SCIATICA (Prescription #2)

1. **Rest and activity modification:** Short-term rest and avoiding activities that worsen the pain.
2. **Physical therapy:** Exercises to strengthen the muscles supporting the spine, improve flexibility, and promote proper posture.
3. **Cap. Pregablin 50mg OR 75mg OR 100mg** (Gabica, Zeegab)
OR **Tab. Lacosamide 50mg OR 100mg OR 150mg** (Lalap, Lecolep)
I - 0 - I (BD), 0 - 0 - I (OD)
4. **Nerve tonic:** **Tab Mecobalamin 500mcg** (Methycobal, Cobalamin)
I - 0 - I (OD)
5. **NSIADs:** **Tab. Naproxen sodium 500mg** (Flexin, Neoprox)
OR **Tab Diclofenac sodium 50mg OR 75mg** (Voren, Voltral)
I - 0 - I (BD)
6. **Gastroprotective:**
↳ **Cap. Omeprazole 40mg** (Risek, Ruling)
↳ OR **Cap. Esomeprazole 40mg** (Nexum, Esso)
0 - 0 - I (OD)
کھانے سے 30 منٹ پہلے



SPINAL STENOSIS

Etiology

Progressive narrowing of the central spinal canal, intervertebral neural foramen, and/or lateral recess (cervical C2 or lumbar spine L1) caused by any of the following:

- ☛ **Degenerative joint disease (most common)**
 - » Spondylolisthesis (anterior or posterior)
 - » Disk space narrowing (e.g., due to osteoarthritis and/or degenerative disk disease)
 - » Facet joint hypertrophy
 - » May affect both the lumbar and cervical spine simultaneously (tandem spinal stenosis)
- ☛ **Iatrogenic:** following spinal surgery such as laminectomy
- ☛ **Systemic disease:** Paget disease, ankylosing spondylitis, tumors
- ☛ **Others:** Trauma, calcification of the ligamentum flavum, uncommon congenital malformations (open spinal dysraphism)

Clinical features

- ☛ **All levels**
 - » Pain is most often gradual onset, chronic, or subacute, depending on the etiology.
 - » Acute pain can occur due to an exacerbation of a chronic underlying process or complication
 - » Radiculopathy (at various affected vertebral levels) often occurs alongside spinal stenosis features, typically due to comorbid etiology, e.g., degenerative disk disease.
- ☛ **Lumbar spinal stenosis**
 - » Load-dependent lower back pain that worsens with walking
 - » **Neuropathic claudication:** a group of neuropathic symptoms affected by postural changes
 - Unilateral or bilateral gluteal, thigh, and calf pain
 - Worsens with lumbar extension (e.g., walking, prolonged standing)
 - Relieved by lumbar flexion (e.g., sitting, laying down, cycling)
 - » Unsteady wide-based gait
 - » Reduced lower extremity reflexes
 - » Mild motor weakness and sensory changes may be present.
 - » Abnormal Romberg test.
- ☛ **Cervical spinal stenosis:** Clinical features are those of myelopathy and vary depending on the level of cord compression. Pain is less common compared with lumbar spinal stenosis.
 - » Neck pain
 - » Gait and balance disturbances
 - » Increased urinary frequency or incontinence
 - » Upper motor neuron signs below the level of stenosis
 - » Lower motor neuron signs at the level of stenosis
 - » **Sensory abnormalities:** pain, paresthesia, &/or anesthesia at or below the level of stenosis; Lhermitte sign
- ☛ **Thoracic spinal stenosis:** As with cervical spinal stenosis, clinical features are those of myelopathy and vary depending on the severity and level of cord compression. They include:
 - » Unilateral or bilateral lower limb paresthesia and pain
 - » Bladder, bowel, and/or sexual dysfunction
 - » Radicular pain around the chest or abdomen
 - » Upper motor neuron signs in the lower limbs

Diagnostic workup

- | | |
|--|--|
| <ul style="list-style-type: none"> ☛ MRI spine plain (without IV contrast): preferred modality in symptomatic patient ☛ CT myelogram: preferred modality in patients with contraindications to MRI or if MRI is inconclusive Supportive Findings: <ul style="list-style-type: none"> » Evidence of spinal stenosis » Narrowing of the spinal canal » Compression of the spinal cord and/or nerve root impingement » Evidence of the underlying cause: degenerative disk disease, facet joint & ligamentous hypertrophy | X-ray spine <ul style="list-style-type: none"> ☛ Indications <ul style="list-style-type: none"> » Routine first-line modality for acute back pain in individuals with no neurological abnormalities » Suspected vertebral fracture ☛ Findings: evidence of the underlying etiology <ul style="list-style-type: none"> » Degenerative joint changes (e.g., loss of disk height, osteophytes, loss of vertebral alignment) » Congenital abnormalities (e.g., scoliosis, lumbosacral transitional vertebrae) » Disk herniation & Hypertrophy of facet joint |
|--|--|





Spinal stenosis - MRI lumbar spine (T2-weighted; sagittal plane)



MRI Lumbar shows spinal stenosis

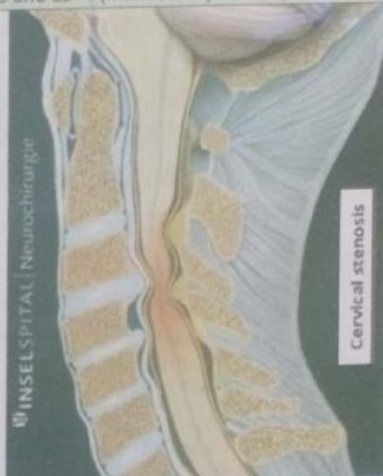


Normal lumbar MRI

Figure: A - Lumbar spinal stenosis: Advanced degenerative changes (red overlay) involve the intervertebral disks and posterior elements at multiple levels. The spinal canal (green overlay) is narrowed at L2-3 and L3-4 (indicated by arrows). White dashed outline: spinal cord



Cervical stenosis



INSESPITAL Neurochirurgie



Spinal stenosis

Treatment of spinal stenosis

Lumbar spinal stenosis

- Mild or moderate symptoms: conservative management with analgesia and physiotherapy
- Significant symptoms or inadequate response to conservative management: Consult neurosurgery for consideration of operative management.
- Conservative management: See below management "Low Back Pain"
- Surgical indication
 - Severe lumbar stenosis
 - Moderate lumbar stenosis with insufficient response to conservative therapy
 - Patients who elect to undergo surgery
- Surgical options to relieve spinal cord compression
 - Laminectomy (decompression surgery)
 - Removal of the dorsal part of the involved vertebra (lamina), thereby relieving the spinal compression
 - Can be combined with vertebral fusion (e.g., in patients with dynamic instability)
 - Laminotomy: minimally invasive removal of part of the lamina
 - Interspinous process spacer devices: Small implants are placed between the spinous processes in a minimally invasive procedure.
 - Outcome: high recurrence rate with all forms of surgical management

Cervical and thoracic spinal stenosis

There is a paucity of evidence on the optimal management of cervical and thoracic stenosis.

- Surgery (decompression with or without vertebral fusion) is preferred in most cases because of the risk of severe neurological symptoms without surgical treatment.
- Conservative management (NSAIDs and/or physiotherapy) may be considered in patients with mild stenosis.



EPIDURAL HEMATOMA (EXTRA-DURAL HEMATOMA "EDH")

Definition: Epidural hematoma occurs as a result of head trauma and subsequent acute hemorrhage, primarily from the middle meningeal artery between the skull and the dura mater. (Blood collection between inner surface of skull and outer (Periosteal) layer of dura).

Etiology: Head injury → middle meningeal artery tear (The middle meningeal artery is a branch of the maxillary artery – serves to supply the skull and the dura)

Location: EDHs are generally U/L > 95% of cases, however, B/L Or multiple EDHs are reported.

> 95% are supratentorial: Temporoparietal (60%), Frontal (20%), and Parieto-occipital (20%)

< 5% are located infratentorially in posterior fossa

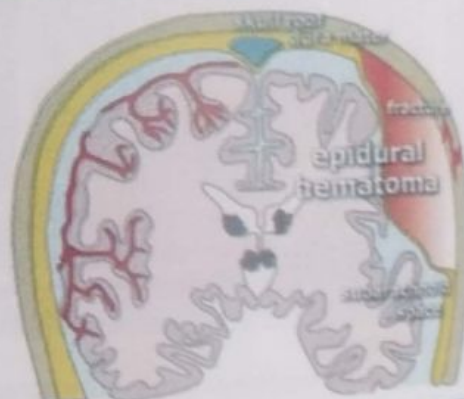
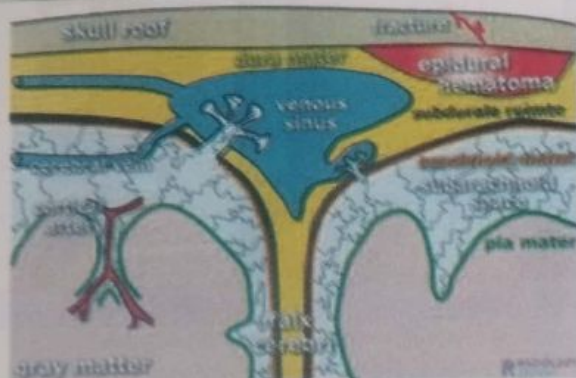
Special locations to consider, particularly those related to venous extradural bleeding, include:

» Vertex EDH (which displaces the superior sagittal sinus)

» Anterior middle cranial fossa: Likely venous bleeding (sphenoparietal sinus), Do not cause midline shift or herniation, rarely grow, can be managed conservatively

Pathophysiology

- The epidural space is a potential space between the dura mater and the calvarium. EDH results from brief linear contact force to the calvarium that causes separation of the periosteal dura from the bone and disruption of interposed vessels due to sheering stress skull fracture are found in 85% - 95 % of adult cases
- Head trauma (usually severe)** → skull fracture (often temporal bone) → rupture of a middle meningeal artery → ↑ intracranial pressure → CN-III palsy, herniation
- Head injury leads to a tear in the middle meningeal artery, leading to rapid filling in the epidural space, which compresses the parenchyma of the brain
 - » Brain parenchymal compression can lead to transtentorial brain herniation
 - » The petrosal bone is thin, which can be easily fractured, resulting in an MMA tear
- Nontraumatic causes of epidural hematoma are very rare.



Clinical features

Typical clinical course

- Initial loss of consciousness following head trauma
- Temporary recovery of consciousness (lucid interval)
 - » Lucid Interval — characterized by recovery of the patient's consciousness, followed by clinical deterioration due to expansion of the hematoma that's under arterial pressure expansion of the hematoma can result in
 - » Ipsilateral dilated pupil (secondary to uncal herniation)
 - » Cushing reflex (hypertension, bradycardia, & resp. depression)
- Renewed decline in mental status

Elevated intracranial pressure

- Headache, Nausea and vomiting
- Ipsilateral anisocoria
- Hypertension, bradycardia, and respiratory irregularity (Cushing's reflex)
- Contralateral focal symptoms/hemiplegia
- Impaired mental status, seizures, coma
 - » Clinical signs of skull fracture (e.g., local hematoma, swelling, laceration)
 - » Symptoms may appear directly after trauma or after a lucid interval

Diagnostics

- Investigation of choice:** CT Brain plain (non-contrast) → Biconvex, hyperdense lesion (that does not cross the suture lines)
 - » Most epidural hematomas are located in the temporoparietal junction and are sharply demarcated.
 - » Hematomas are limited by suture lines.
 - » In some cases, an accompanying cranium fracture may be seen.



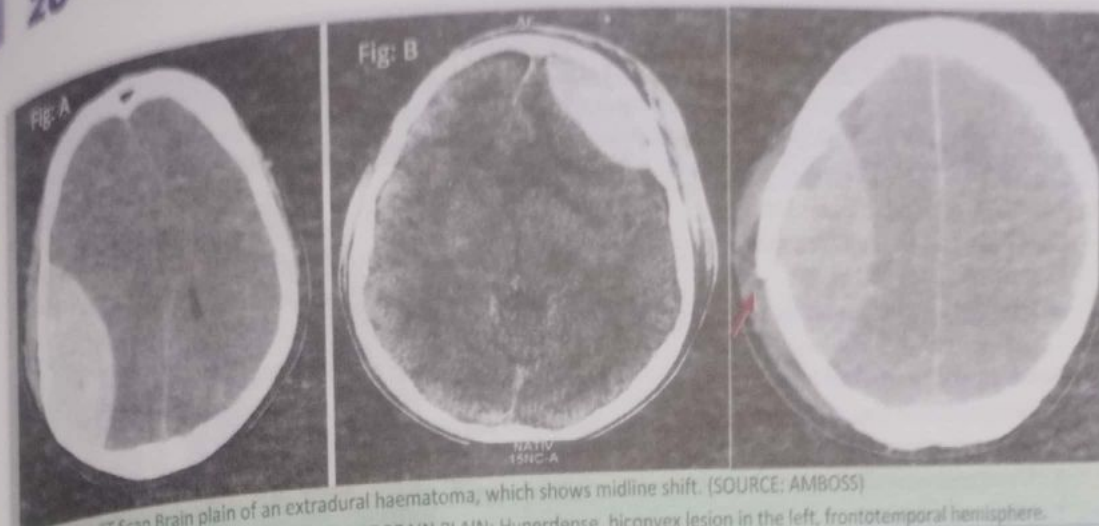


Figure A – CT Scan Brain plain of an extradural haematoma, which shows midline shift. (SOURCE: AMBOSS)

Figure B – LEFT FRONTOTEMPORAL EDH ON CT BRAIN PLAIN: Hyperdense, biconvex lesion in the left, frontotemporal hemisphere.

TREATMENT OF EXTRA-DURAL HEMATOMA (EDH)



EDH is one of the most urgent neurosurgical emergencies that may need prompt evacuation.

- ✓ Admit in ICU/HDU, urgent neurosurgical consult for consideration of surgical intervention
- ✓ Stabilize patients using ABCD&E approach.
- ✓ Establish large-bore intravenous (IV) access.
- ✓ Anticoagulation: Stop all anticoagulants, antiplatelet agents. Identify and treat any underlying coagulopathy.
- ✓ Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂.
- ✓ Obtained investigations: CBC, Urea, Creatinine, Electrolytes, LFTs, PT APTT & INR, RBS/Blood glucose
- ✓ IV fluids therapy: Ringer lactate (R/L) x 1L and 0.9% N.S x 1L x IV x BD/TDS. Recommended maintenance fluids around 30-35ml/kg/day for adults. Adjust fluid therapy based on individual patient factors such as age, comorbidities (e.g., heart failure, renal impairment), and hemodynamic status.
- ✓ Glycemic control: For secondary brain injury prevention
 - » Hypoglycemia: Manage, if blood glucose is < 60 mg/dL.
 - » Hyperglycemia: Manage and keep blood glucose levels between 140 to 180 mg/dL
- ✓ Controlling Elevated Intracranial hypertension (ICP): Treat by elevating head-end of the bed to 30°, starting hypertonic saline or mannitol, and hyperventilating the patient.
MANNITOL IS CLINICALLY AVOIDED/Mannitol Is Contraindicated in EDH → EDH is already known as expanding hematoma; by giving Mannitol ICP & Brain Edema will decrease → will lead to brain Shrinkage → it will provide more space to bleeding and EDH will increase.
- ✓ Blood pressure: Systolic B.P between 150 and 220 mmHg, acute lowering of systolic B.P to a target of 140 mmHg with the goal of maintaining in the range of 130 to 150 mmHg is safe. **Avoid hypotension (MAP < 65 mm Hg).**
 - ✦ Inj. Labetalol 50mg/10ml x 20mg x IV once, then 20-80mg IV every 10 minutes, titrated as needed.
 - ✦ OR Inj. Hydralazine 20mg/1ml x diluted in 0.9% NS, loading dose 10-20mg over 5-10 min, then repeat after 20 min if desire BP is not achieved. (for more detail see hypertensive emergency – ER SECTION)
- ✓ With vomiting – consider ONE of the following anti-emetics:
 - ✦ Inj. Metoclopramide 10mg/2ml (Metaclo, Maxolon) x IV x TDS
 - ✦ OR Inj. Dimenhydrinate 50mg/ml (Gravinate) x IV x TDS
 - ✦ OR Inj. Ondansetron 8mg/4ml (Onset, Onseron) x diluted in 50-100 ml of 0.9% NS OR D5%W, IV over 15 minutes.
- ✓ Gastroprotective: Inj. Omeprazole 40mg (Ruling, Risek) diluted in 100ml 0.9% NS x IV x OD
- ✓ Antibiotic prophylaxis: Inj. Ceftriaxone 2g (Oxidil, Rocephin) x IV x OD
- ✓ With seizures: Inj. Diazepam 10mg/2ml (Valium) diluted in 8ml 0.9% NS x at dose 5-10mg (5-10ml) IV, may repeat if required. If unresponsive then treat it as status epilepticus (see status epilepticus). **For seizures prophylaxis: Inj. Levetiracetam 500mg/5ml (Lerace, Epilapsa) at dose 1-2g in 100ml 0.9% NS x IV over 15-20 min**
- ✓ With fever/pain: Inj. Paracetamol 1g/100ml (Provas) x IV x TDS/SOS OR PO Tab. Panadol 500-1000mg x TDS/QID

Surgical management: First-line: urgent craniotomy and hematoma evacuation. Second-line: emergency burr hole

Prognosis: 1. Mortality rate: depends on preoperative condition. 2. Factors associated with a worse prognosis: Low Glasgow Coma Scale scores before surgical intervention, Delay in treatment and Age > 75 years

Complications: 1. Transtentorial herniation. 2. Respiratory failure and death



SUBDURAL HEMATOMA (SDH)

Definition: SDH refers to bleeding between the dura mater and arachnoid membrane. It is caused by head trauma that results in a tear in the bridging vein, which connects the superficial cerebral veins to the dural venous sinuses.

Etiology

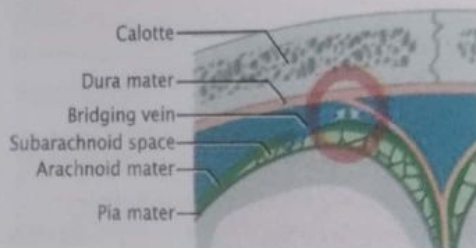
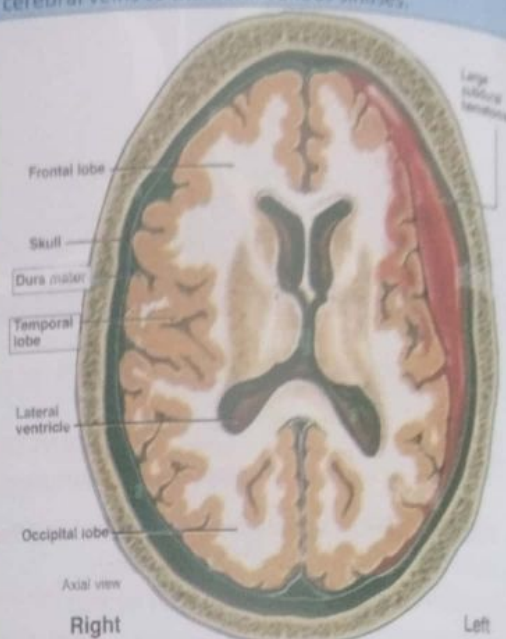
- » Rupture of the bridging veins caused by:
 - » Blunt head trauma (most common)
 - Shaken baby syndrome
 - Frequent falls: due to old age, alcohol abuse, epilepsy, and hyponatremia
 - » Nontraumatic intracranial hemorrhage
 - Anticoagulation therapy or coagulopathy
 - Ruptured intracranial aneurysm
 - Arteriovenous malformation
 - Intracranial tumors
 - » Idiopathic, or iatrogenic (i.e., surgical) causes
- » Subdural hematoma (SDH) may occur after trivial trauma in patients with multiple risk factors!

Classification

- It is based on the onset of symptoms after the inciting event
- » Acute SDH: immediately after trauma or rapidly within 72hr
 - » Subacute SDH: 4–21 days after trauma
 - » Chronic SDH: > 21 days after trauma

Pathophysiology

- » SDH is a form of intracranial hemorrhage in which blood accumulates between the dura mater and arachnoid membrane. → Tearing in bridging veins → low-pressure venous bleeding.



Clinical features

Clinical features depend on the size and location of the hematoma and the length of time since the inciting event.

Acute SDH

1. **Symptom onset:** Typically, immediately after (or within 3 days of) the inciting event
2. **Progression:** Rapid, can progress to cerebral herniation and death
3. **Clinical features**
 - » Impaired consciousness and confusion, rapidly deteriorating to coma
 - » Focal neurological signs, such as: 1. Contralateral hemiparesis and UMN signs. 2. Ipsilateral hemiparesis due to Kernohan syndrome (false localizing sign; uncommon). 3. CN palsies, manifesting as: Diplopia, Blurred vision, Unequal pupils and Anosmia. 4. Slurred and/or disorganized speech
 - » Pupillary abnormalities; e.g., anisocoria, unilateral or bilateral fixed dilated pupils
 - » Manifestations of ↑ ICP, such as: Headache, Vomiting and Cushing triad
 - » Signs of cerebral herniation syndromes
 - » Abnormal posturing (e.g., decorticate posturing, decerebrate posturing), Seizures

Subacute SDH

1. **Symptom onset:** 4–20 days after the inciting event, can be acute or insidious
2. **Progression:** A rebleed can cause rapid neurological decline.
3. **Clinical features:** a combination of features of acute SDH and chronic SDH.

Chronic SDH



1. Symptom onset: Insidious, ≥3 weeks after the inciting event
2. Progression: typically, gradual
3. Clinical features
 - » ALOC that can progress to coma, characterized by: Confusion, Delirium, Excessive drowsiness
 - » Recurrent headaches
 - » Cognitive deficits: Impaired memory, Dementia
 - » Focal neurological signs: Contralateral hemiparesis (most common) that can progress to hemiplegia, Incontinence
 - » Ataxia, recurrent falls, changes in personality and seizures.

Diagnostic workup

- Diagnosis is made on Brain radiograph
 - » Investigation of choice: CT scan brain plain (non-contrast)
 - » MRI is indicated when CT scan is inconclusive but suspicion for subdural hematoma is high.

Appearance on brain imaging

- » Crescent-shaped, concave hemorrhage that crosses suture lines but not the midline
- » Varies depending on clot age and organization:

SDH type	CT features	MRI features
Acute SDH	Hyperdense with respect to the cortex	Hypointense to isointense with respect to grey matter
Subacute SDH	Isodense with respect to the cortex after 10–14 days	Mostly hyperintense
Chronic SDH	Hypodense with respect to the cortex and may appear isodense with respect to cerebrospinal fluid	Mostly isointense with respect to cerebrospinal fluid

Note: Traumatic acute SDH and acute EDH have similar clinical manifestations and are indistinguishable without neuroimaging.

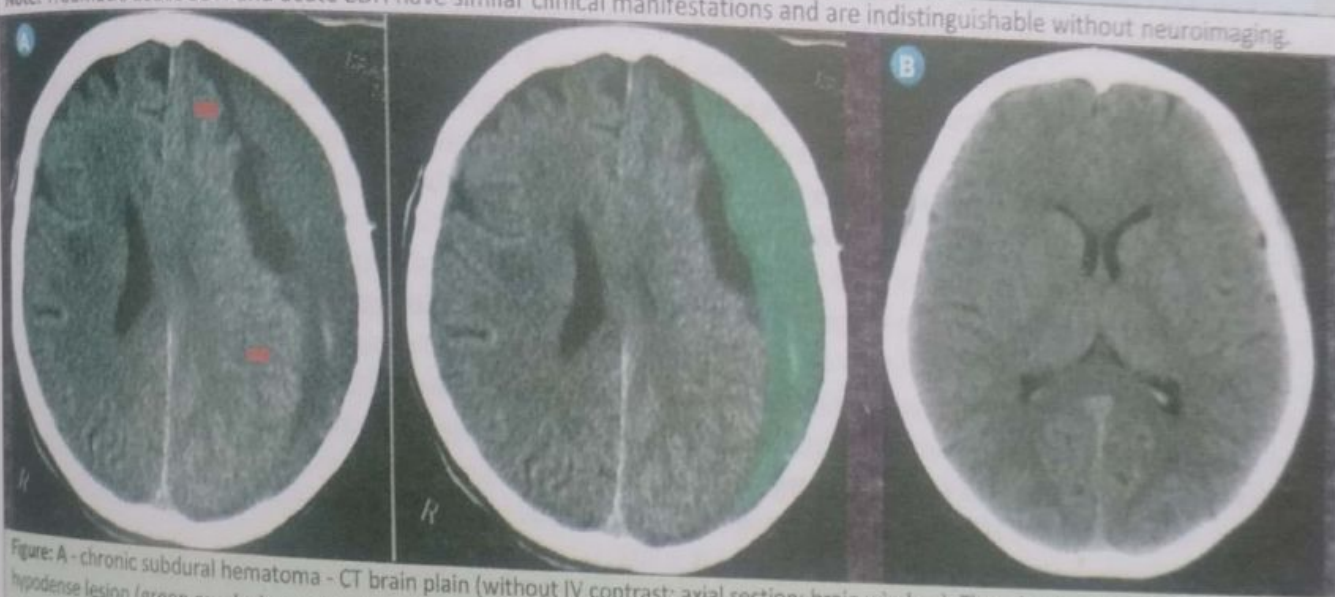


Figure A - chronic subdural hematoma - CT brain plain (without IV contrast; axial section; brain window): There is a large, crescent-shaped, hypodense lesion (green overlay) over the lateral aspect of the left hemisphere that crosses cranial sutures. Mass effect of the lesion is visible as compression of the left lateral ventricle. These findings are characteristic of a large chronic subdural hematoma.

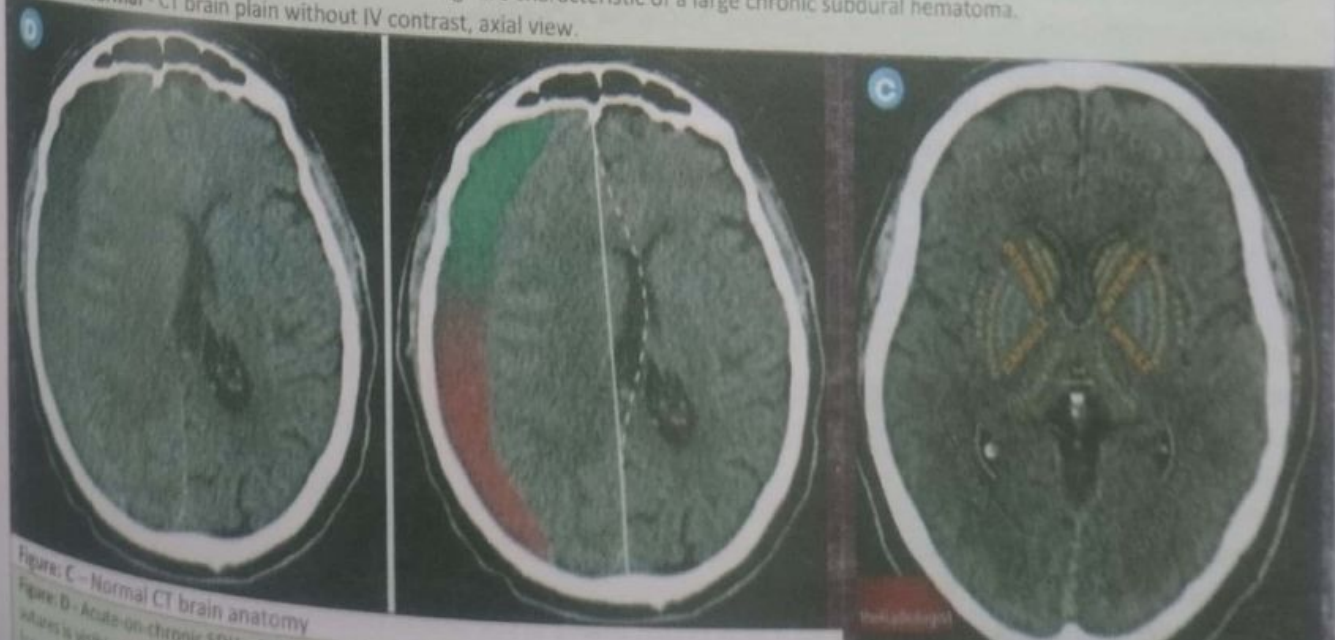


Figure C - Normal CT brain anatomy
Figure D - Axial on chronic SDH - CT brain plain (without IV contrast; axial section; brain window): There is a large, crescent-shaped, hypodense lesion (green overlay) over the lateral aspect of the left hemisphere that crosses cranial sutures. Mass effect of the lesion is visible as compression of the left lateral ventricle.

recent hemorrhage into the existing hematoma (recent blood clots contain concentrated hemoglobin, which is hyperdense). Mass effect is visualized as a shift of the midline (white line) to the left (dashed white line), compression of the left lateral ventricle, and compression of the adjacent cerebral parenchyma, which appears edematous (hyperdense with loss of the sulci and gyri).



TREATMENT OF SUB-DURAL HEMATOMA (SDH)

Conservative treatment: Indicated if no clinical signs of herniation are present and the neurological status is stable, midline shift $<5\text{mm}$, and the hematoma is $<10\text{mm}$. Monitoring with serial of brain CT scans

- Admit in ICU/HDU, urgent neurosurgical consult for consideration of surgical intervention and ICP monitoring.
- Stabilize patients using ABCD&E approach.
- Establish large-bore intravenous (IV) access.
- Anticoagulation: Stop all anticoagulants, antiplatelet agents. Identify and treat any underlying coagulopathy.
- Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂.
- Obtained investigations: CBC, Urea, Creatinine, Electrolytes, LFTs, PT APTT & INR, RBS, & ABGs.
- IV fluids therapy: Ringer lactate (R/L) x 1L and 0.9% N.S x 1L x IV x BD/TDS. Recommended maintenance fluids around 30-35ml/kg/day for adults. Adjust fluid therapy based on individual patient factors such as age, comorbidities (e.g., heart failure, renal impairment), and hemodynamic status.
- Glycemic control: For secondary brain injury prevention
 - » Hypoglycemia: Manage, if blood glucose is $<60\text{ mg/dL}$.
 - » Hyperglycemia: Manage and keep blood glucose levels between 140 to 180 mg/dL.
- Controlling Elevated intracranial hypertension (ICP): Treat by elevating head-end of the bed to 30°, starting hypertonic saline or mannitol, and hyperventilating the patient.

Mannitol infusion 20%/500ml (=100 grams) x **Initial dose:** 0.25–1.5 g/kg IV as a single dose (for 70 kg patients' weight, the initial dose = 87.5–525ml) over 30 to 60 minutes, with effects usually seen within 5 to 10 minutes and lasting up to about 6 hours. **Maintenance dose:** 0.25-0.5 g/kg IV every 6 hours or as needed. **Dosage:** should be adjusted according to the patient's age, body weight, and renal function.
- Blood pressure: Systolic B.P between 150 and 220 mmHg, acute lowering of systolic B.P to a target of 140 mmHg with the goal of maintaining in the range of 130 to 150 mmHg is safe. **Avoid hypotension (MAP $<65\text{ mmHg}$).**
 - ❖ Inj. Labetalol 50mg/10ml x 20mg x IV once, then 20-80mg IV every 10 minutes, titrated as needed.
 - ❖ OR Inj. Hydralazine 20mg/1ml x diluted in 09 ml 0.9% NS, loading dose 10-20mg over 5-10 min, then repeat after 20 min if desire BP is not achieved. (for more detail see hypertensive emergency – ER SECTION)
- With vomiting – consider ONE of the following anti-emetics:
 - ❖ Inj. Metoclopramide 10mg/2ml (Metaclo, Maxolon) x IV x TDS
 - ❖ OR Inj. Dimenhydrinate 50mg/ml (Gravinate) x IV x TDS
 - ❖ OR Inj. Ondansetron 8mg/4ml (Onset, Onseron) x diluted in 50-100 ml of 0.9% NS OR D5%W, IV over 15 minutes.
- Gastroprotective: Inj. Omeprazole 40mg (Ruling, Risek) diluted in 100ml 0.9% NS x IV x OD
- Antibiotic prophylaxis: Inj. Ceftriaxone 2g (Oxidil, Rocephin) x IV x OD
- With seizures: Inj. Diazepam 10mg/2ml (Valium) diluted in 8ml 0.9% NS x at dose 5-10mg (5-10ml) IV, may repeat if required. If unresponsive then treat it as status epilepticus (see status epilepticus). **For seizures prophylaxis:** Inj. Levetiracetam 500mg/5ml (Lerace, Epilapsa) at dose 1-2g in 100ml 0.9% NS x IV over 15-20 min
- With fever/pain: Inj. Paracetamol 1g/100ml (Provas) x IV x TDS/SOS OR PO Tab. Panadol 500-1000mg x TDS/QID

Surgical management

- **Surgical decompression:**

Indications (Only one of the following criteria must be met.)

 - » Clinical signs of herniation
 - » Unstable neurologic status
 - » Midline shift $>5\text{ mm}$
 - » Hematoma $>10\text{ mm}$
- **Procedures**
 - » **Trephination and drainage of hematoma:** A burr hole is drilled in the skull & the hematoma is drained.
 - » **Craniotomy and evacuation of hematoma:** A bone flap is removed from the skull & the hematoma is evacuated.
- **Prognosis:** The prognosis of chronic SDH is better than that of acute SDH.



SUBARACHNOID HEMORRHAGE (SAH)

Clinical features

- ☛ **Sudden, Severe Headache (Thunderclap headache):** Often described as the worst headache of one's life.
- ☛ **Neurological symptoms:** such as altered mental status, confusion, or loss of consciousness.
- ☛ **Meningeal signs:** Neck stiffness, Photophobia, Nausea and vomiting, Kernig sign and Brudzinski sign
- ☛ **Signs due to mass effect:** cranial nerve palsy, altered mental status (delirium), focal neurologic deficits, seizures

Diagnostic workup

- ☛ **Best initial test:** CT scan Brain
- ☛ **Lumbar Puncture:** If initial CT scan is negative but suspicion remains high, this may be performed to detect blood (Xanthochromia) in the cerebrospinal fluid (CSF).
- ☛ **CT Angiography (CTA) OR Digital subtraction angiography (DSA):** To locate the source of bleeding, typically performed if an aneurysm is suspected.



TREATMENT OF SUBARACHNOID HEMORRHAGE (SAH)

- ☛ Stabilize patients using ABCD&E approach.
- ☛ Establish large-bore intravenous (IV) access.
- ☛ **Vitals monitoring:** Check BP, PR, RR, Temperature, SpO₂.
- ☛ **Obtained investigations:** CBC, Urea, Creatinine, Electrolytes, LFTs, PT APTT & INR and blood glucose/RBS.
- ☛ **IV fluids therapy:** Ringer lactate (R/L) x 1L and 0.9% N.S x 1L x IV x BD/TDS. Recommended maintenance fluids around 30-35ml/kg/day for adults. Adjust fluid therapy based on individual patient factors such as age, comorbidities (e.g., heart failure, renal impairment), and hemodynamic status.
- ☛ **Prevent cerebral vasospasm in all patients**
 - ☛ **Tab. Nimodipine 30mg** (Bredin, Nimotop) x at dose 60mg (2-Tablets) orally every 4 hours for 21 days
 - ☛ **Additionally:** Tab. Cilostazol 100mg (Pletaal) at dose 100mg orally twice daily for 14-21 days (some guidelines recommend this to prevent cerebral vasospasm and improve outcomes.
- ☛ **Controlling Elevated intracranial hypertension (ICP):** Treat by elevating head-end of the bed to 30°, starting hypertonic saline or mannitol, and hyperventilating the patient.
 - Mannitol infusion 20%/500ml** (=100 grams) x **Initial dose:** 0.25–1.5 g/kg IV as a single dose (for 70 kg patients' weight, the initial dose = 87.5–525ml) over 30 to 60 minutes, with effects usually seen within 5 to 10 minutes and lasting up to about 6 hours. **Maintenance dose:** 0.25-0.5 g/kg IV every 6 hours or as needed. **Dosage:** should be adjusted according to the patient's age, body weight, and renal function.
- ☛ **Blood pressure:** Systolic B.P between 150 & 220 mmHg, acute lowering of systolic B.P to a target of 140 mmHg with the goal of maintaining in the range of 130 to 150 mmHg is safe. **Avoid hypotension (MAP < 65 mm Hg).**
 - ☛ **Inj. Labetalol 50mg/10ml** x 20mg x IV once, then 20-80mg IV every 10 minutes, titrated as needed.
 - ☛ **OR Inj. Hydralazine 20mg/1ml** x diluted in 09 ml 0.9% NS, loading dose 10-20mg over 5-10 min, then repeat after 20 min if desire BP is not achieved. (See hypertensive emergency – ER SECTION)
- ☛ **With vomiting – consider ONE of the following anti-emetics:**
 - ☛ **Inj. Metoclopramide 10mg/2ml** (Metaclo, Maxolon) x IV x TDS
 - ☛ **OR Inj. Dimenhydrinate 50mg/ml** (Gravinate) x IV x TDS
 - ☛ **OR Inj. Ondansetron 8mg/4ml** (Onset, Onseron) x diluted in 50-100 ml of 0.9% NS OR D5%W, IV over 15 min.
- ☛ **Gastroprotective:** **Inj. Omeprazole 40mg** (Risek, Ruling) diluted in 100ml 0.9% NS x IV x OD
- ☛ **Antibiotic prophylaxis:** **Inj. Ceftriaxone 2g** (Oxidil, Rocephin) x IV x OD
- ☛ **With seizures:** **Inj. Diazepam 10mg/2ml** (Valium) diluted in 8ml 0.9% NS x at dose 5-10mg (5-10ml) IV, may repeat if required. If unresponsive then treat it as status epilepticus (see status epilepticus). **For seizures prophylaxis:** **Inj. Levetiracetam 500mg/5ml** (Lerace, Epilapsa) at dose 1-2g in 100ml 0.9% NS x IV over 15 min
- ☛ **Pain control/analgesia:**
 - ☛ **Inj. Paracetamol 1g/100ml** (Provas, Paracet) x IV x TDS/SOS
 - ☛ **OR Inj. Tramadol 100mg/2ml** (Tramol) **OR Inj. Nalbuphine 10mg/ml** (Kinz) + **Adjunct:** **Inj. Metoclopramide 10mg/2ml** (Metaclo) or **Inj. Dimenhydrinate 50mg/1ml** (Gravinate) dilute in 100ml 0.9% NS.
- ☛ **Neuroprotective:** **Inj. Alphacholine (Neurocholine)** 500mg-1g x IV x BD
- ☛ **Surgical Intervention:** Often required to clip or coil the ruptured aneurysm, which is the most common cause of subarachnoid hemorrhage (SAH)



BRAIN ABSCESS

PATHOPHYSIOLOGY OF BRAIN ABSCESS

- ☞ **Initial infection:** entry of pathogens via contiguous spread, direct inoculation, or hematogenous spread can result in the following
 - » **Early cerebritis**
 - Occurs during the first 3–5 days
 - Infiltration of neutrophils and cerebral edema
 - » **Late cerebritis**
 - Occurs after 2–3 weeks
 - Necrosis, liquefaction, and infiltration of macrophages
 - Eventually results in the formation of a fibrotic capsule around the lesion
 - » **Spread patterns**
 - Hematogenous spread of pathogens is associated with multiple brain abscesses.
 - Single abscess is associated with contiguous spread (e.g., otitis media/mastoiditis).
- ☞ **Common sites of contiguous spread**
 - » Temporal lobe and cerebellum (from otogenic infections)
 - » Frontal lobe (from sinus infections)

Clinical features

- ☞ Clinical features depend on the size and location of the lesion.
- ☞ **Dull persistent headache:** a ruptured abscess is associated with a sudden worsening of headache and meningism
- ☞ **Focal neurological deficits:** commonly oculomotor nerve palsy or abducens nerve palsy secondary to increased ICP (e.g., weakness, speech difficulties)
- ☞ **Symptoms of increased intracranial pressure (ICP):** Vomiting, Papilledema, Altered mental status
- ☞ **Fever**
- ☞ **Seizures:** Generalized or focal seizures

Diagnostics workup

- ☞ **Laboratory tests:**
 - » **Inflammatory markers:** ↑ CRP, ↑ ESR
 - » **CBC:** Leukocytosis
 - » **Blood cultures** to identify the causative organism
 - » **Lumbar puncture (CSF Analysis):** Generally avoided. Contraindicated in the presence of raised intracranial pressure (risk of brain/uncal herniation), which can be accessed via imaging.
 - » **Typical findings** include elevated protein, normal or decrease glucose, sterile cultures, and raised WCC
- ☞ **Imaging: CT scan or MRI**
 - » Best initial diagnostic test
 - » Used to confirm the diagnosis and to localize the lesion (as well as size and number of lesions)
 - » Can be used to monitor response to treatment
 - » **Findings include:** intraparenchymal lesions with a central hypodense (necrotic) area and peripheral ring enhancement
 - **T1-weighted with contrast agent:** Central hypointense (necrotic) lesions with ring-formed contrast enhancement, potentially in the perifocal hypointense regions (perifocal edema)
 - **T2-weighted:** Central hyperintense region (necrosis) with an isointense rim and perifocal hyperintense regions (perifocal edema)
 - **Diffusion-weighted imaging (DWI):** hyperintense areas
- ☞ **Best confirmatory test → Biopsy (and drainage):** microscopic examination and culture
 - » Entails either craniotomy for complete excision or image-guided aspiration
 - » Distinguishes an abscess from a tumor
 - » Cultures also determine the infective organism and its antibiotic sensitivities.
- ☞ **Electroencephalography:** striking focal lesions with potential for epileptic seizures



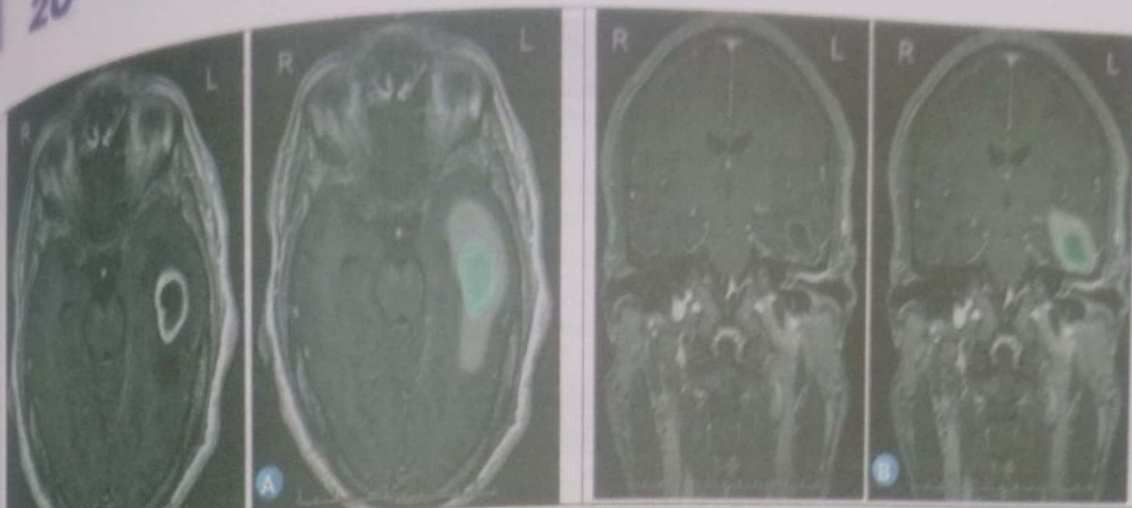


Figure A - MRI (with contrast, axial view) - shows an oval lesion can be seen in the left temporal lobe, with ring-like contrast enhancement (green ring) and central necrosis (green overlay). The perifocal edema (white overlay) that is visible corresponds to the lesion. [Source - AMBOSS]

Figure B - MRI Brain (with contrast; coronal plane) - shows Ring-enhancing lesion left temporal lobe, in the left temporal lobe, there is an oval lesion with ring-like contrast enhancement (green outline), central low signal intensity necrosis (green hatching), and perifocal edema (white area).



TREATMENT OF BRAIN ABSCESS

- ▣ Stabilize patients using ABCD&E approach.
- ▣ Establish large-bore intravenous (IV) access.
- ▣ Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂.
- ▣ Obtained investigations: CBC, Urea, Creatinine, Electrolytes, LFTs, PT APTT & INR and blood glucose/RBS.
- ▣ IV fluids therapy: Ringer lactate (R/L) x 1L and 0.9% N.S x 1L x IV x BD/TDS. Recommended maintenance fluids around 30-35ml/kg/day for adults. Adjust fluid therapy based on individual patient factors such as age, comorbidities (e.g., heart failure, renal impairment), and hemodynamic status.
- ▣ Management of Cerebral edema: Inj. Dexamethasone 4mg/1ml (Decadron) at dose 10mg, IV loading dose, followed by 4mg, IV, every 6 hours.
- ▣ Initial empirical antibiotics therapy:
 - ▣ Inj. Ceftriaxone 2g (Oxidil, Rocephin, Titan) x IV x every 12 hours (BD)
 - ▣ PLUS, Inj. Metronidazole 500mg/100ml (Flagyl) x IV x every 8 hours (TDS)
 - ▣ PLUS, Inj. Vancomycin 500mg at dose 15-20mg/kg IV every 8-12 hours x IV x TDS
 - ✓ Antibiotic therapy for specific pathogen should be initiated after culture results
 - ✓ If fungal infection is suspected: Antifungal therapy with IV Amphotericin-B as dosage depending on formulation, typically 0.7-1mg/kg/day, x IV
- ▣ With seizures: Inj. Diazepam 10mg/2ml (Valium) diluted in 8ml 0.9% NS x at dose 5-10mg (5-10ml) IV, may repeat if required. If unresponsive then treat it as status epilepticus (see status epilepticus). For seizures prophylaxis: Inj. Levetiracetam 500mg/5ml (Lerace, Epilapsa) at dose 1-2g in 100ml 0.9% NS x IV over 15 min
- ▣ Pain control/analgesia:
 - ▣ Inj. Paracetamol 1g/100ml (Provas, Paracet) x IV x TDS/SOS
 - ▣ OR Inj. Tramadol 100mg/2ml (Tramol) OR Inj. Nalbuphine 10mg/ml (Kinz) + Adjunct: Inj. Metoclopramide 10mg/2ml (Metaclon) or Inj. Dimenhydrinate 50mg/1ml (Gravinate) dilute in 100ml 0.9% NS.
- ▣ Gastroprotective: Inj. Omeprazole 40mg (Risek, Ruling) x IV x OD
- ▣ With vomiting - consider ONE of the following anti-emetics:
 - ▣ Inj. Metoclopramide 10mg/2ml (Metaclon, Maxolon) x IV x TDS
 - ▣ OR Inj. Dimenhydrinate 50mg/ml (Gravinate) x IV x TDS
 - ▣ OR Inj. Ondansetron 8mg/4ml (Onset, Onseron) x diluted in 50-100 ml of 0.9% NS OR D5%W, IV over 15 min.

Surgical Intervention

- ▣ Aspiration: Stereotactic or open aspiration to reduce intracranial pressure and obtain material for diagnosis.
- ▣ Excision: Indicated for large abscesses, multiloculated abscesses, or those not responding to aspiration and antibiotics.



HYDROCEPHALUS

- Definition: Hydrocephalus refers to the abnormal enlargement of cerebral ventricles and/or subarachnoid space as a result of excessive cerebrospinal fluid (CSF) accumulation, resulting from a disturbance of its flow, absorption or, uncommonly, secretion. In hydrocephalus ICP can be increased or normal.
- Types: There are two types of true hydrocephalus:
 - Communicating hydrocephalus, which occurs due to decreased CSF absorption or increased CSF production in absence of any CSF-flow obstruction.
 - Non-communicating hydrocephalus, which occurs due to the obstructed passage of CSF from the ventricles to the subarachnoid space.

Overview/classification of hydrocephalus

Type	Pathophysiology	Clinical features
Communicating hydrocephalus	↑ CSF production ↓ CSF absorption	Typical findings of raised ICP: Headache, nausea, and vomiting, Papilledema, CN-VI palsy, Abnormal gait Impaired consciousness, Cushing triad (irregular breathing, widening pulse pressure, bradycardia)
Noncommunicating hydrocephalus	Obstructed passage of CSF from the ventricles to the subarachnoid space	Classic triad: urinary incontinence, dementia & ataxic gait (frequent falls, broad-based gait with short steps)
Normal pressure hydrocephalus (NPH)	↓ CSF absorption	Symptoms of the underlying condition (e.g., Alzheimer disease, Pick disease)
Hydrocephalus ex vacuo	Loss of brain tissue	

Diagnostic workup

- Ultrasonography: Indication - Clinical suspicion during antenatal period or in infants < 6 months of age (through the anterior fontanelle when it is still open). Findings: enlarged lateral ventricles
- MRI or CT scan: Indication - 1. Older infants: when fontanelle is already closed, typically infants > 6 months of age (MRI is preferred to CT) & 2. Adults. Findings: Enlarged ventricles, Mickey Mouse ventricles. If the lateral ventricles and 3rd ventricle are all very dilated, & the 4th ventricle is small, it is likely that the obstruction is at the level of the aqueduct of Sylvius.

Clinical features

Features of increased intracranial pressure (ICP)

- Headache, nausea, and vomiting
- Papilledema
- Abnormal gait
- Impaired consciousness
- Cushing triad (irregular breathing, widening pulse pressure, bradycardia)
- Abducens (6th CN) nerve palsy

Additional features in infants

- Macrocephaly: an enlarged head with a circumference greater than the average for age and sex by two standard deviations (as indicated by a percentile growth chart)
- Tense fontanelle
- Setting sun sign: persistent downward deviation of the eyes due to increased ICP in infants and young children
- Developmental delays (e.g., psychomotor delays)
- Behavioral changes (e.g., irritability)
- MacEwen sign (cracked pot sign): percussion of the skull near the junction of the frontal, temporal, and parietal bones evoke an unusually resonant sound
- Caused by separation of cranial sutures due to raised ICP
- Found in late hydrocephalus

Other findings

- Changes in vital signs resulting from brainstem compression due to herniation
- Lower extremity spasticity, hyperreflexia

Rx

- Most types of hydrocephalus are progressive and carry a risk of neurological damage.
- Definitive treatment of hydrocephalus involves the drainage of excess CSF via a cerebral shunt, usually into the peritoneum (ventriculoperitoneal or VP shunt).

Treatment option include:

1. Cerebral shunt (Ventriculoperitoneal shunt)

- meticulous sterile technique, including the use of a 'no touch' technique of the shunt and total avoidance of skin contact with the shunt
- Intra-operative prophylactic antibiotics

2. Possible interim therapy

- Acetazolamide
- Diuretics (Furosemide)
- Serial lumbar punctures
- Fibrinolysis

3. Alternative surgical procedures

- Endoscopic 3rd ventriculostomy
- Choroid plexectomy (or coagulation)
- Cerebral aqueductoplasty: a procedure in which a stenotic or closed cerebral aqueduct is opened to allow adequate passage of CSF between the 3rd and 4th ventricles.



CEREBRAL SHUNT (VENTRICULOPERITONEAL OR VP SHUNT)

Definition

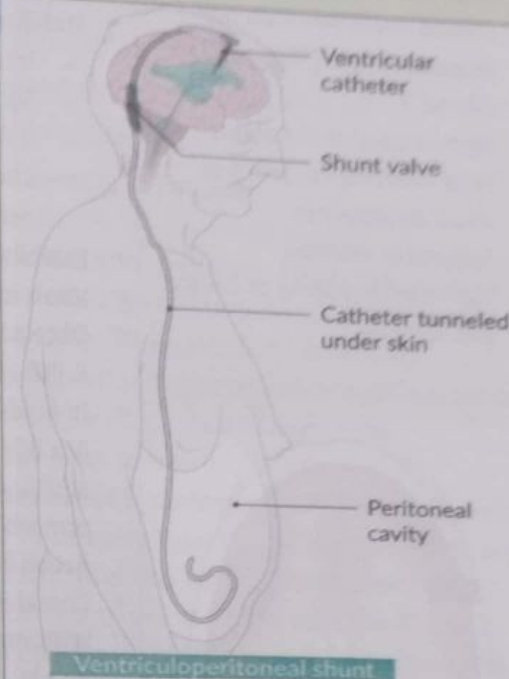
Shunt is a long-term treatment for hydrocephalus intended to return excess cerebrospinal fluid from the ventricle to systemic circulation, most commonly through the peritoneum.

Important component

1. Inflow catheter
2. Adjustable one-way pressure valves
3. Outflow catheter
4. Reservoir

Complications

- Shunt infection: Bacterial contamination (Staph. epidermidis), often associated with biofilm formation
- Obstruction of the shunt
- Shunt malfunction (partial or complete blockage of the shunt)
- Underdrainage (CSF not removed quickly enough) → raised ICP
- Overdrainage (drainage of too much CSF): Intracranial hypotension syndrome
- Slit ventricle syndrome: it is due to chronic overdrainage of CSF
 - Pathophysiology of slit ventricle syndrome: The exact mechanisms underlying this syndrome are still debated. One hypothesis states that the overdrainage of one ventricle results in the collapse of its walls and occlusion of the shunt catheter. This, in turn, leads to underdrainage of the contralateral ventricle.
 - Clinical features of Slit ventricle syndrome
 - Chronic intermittent headache
 - Nausea/vomiting
 - Altered mental status
 - Cranial neuropathies



CERVICAL SPINE DISTORTION (WHIPLASH INJURY)

- Definition: Whiplash is an injury to your neck. It is caused by your neck bending forcibly forward and then backward, or vice versa. Poorly understood, usually involves the muscles, discs, nerves, & tendons in your neck.
- Etiology: often seen after car accidents due to abrupt flexion/extension movement of the neck
- Diagnostic workup
 - X-ray of the cervical spine.
 - CT scan/MRI on suspicion of changes in the spinal canal and neurologic deficits.
 - Doppler ultrasound if injury to vessels in the neck is suspected.
- Treatment
 - Uncomplicated distortion
 - If necessary, short-term NSAIDs and muscle relaxant to treat muscular tension
 - Active exercise treatment
 - In case of fractures or spinal cord lesions: surgery

△ Whiplash injury

C/C:

- Headache, neck ache, and/or pain radiating into the back of the head, the shoulders, or the arms
- Pain-based reduction in neck range of motion and palpable muscle tension of the shoulders and neck, as well as arm and hand paresthesia
- General symptoms such as dizziness, nausea, fatigue, insomnia, tinnitus, and problems with concentration.

Rx

TREATMENT OF WHIPLASH INJURY

(Voren, Voltral)

1. Short term NSAIDs: Tab. Diclofenac sodium 50mg
OR Tab. Naproxen sodium 500mg (Flexin, Neoprox)
1-0-1 (BD)
2. Muscle relaxants: Tab. Tizanidine 2mg (Movax, Ternalin)
OR Tab. Eperisone 50mg (Myonal, Perispa, SMUR)
0-0-1 (OD) OR 1-0-1 (BD)
3. Gastroprotective: Cap. Omeprazole 40mg (Risek, Ruling)
0-0-1 (OD) 30 منٹ پہلے

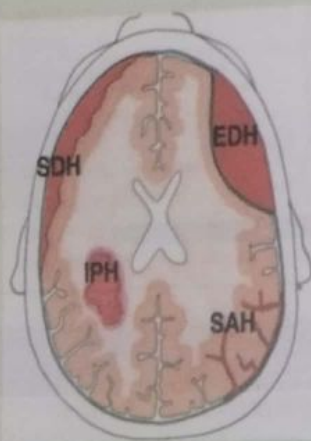


TRAUMATIC BRAIN INJURY (HEAD TRAUMA)

△ Traumatic Brain Injury (TBI)
C/C:

Red Flag Signs in head injury

- » Impaired consciousness level
- » Dilated pupils which do not respond to light ("fixed and dilated")
- » Signs of basal skull fracture
- » Focal neurological deficit or visual disturbances
- » Seizures or amnesia
- » Significant headache or nausea and vomiting



TREATMENT OF TRAUMATIC BRAIN INJURY (TBI)

Rx

- Early referral to neurosurgery. HDU/ICU admission
- Urgent CT scan brain plain and CT scan of cervical spine
- Stabilize patients using ABCD&E approach.
 - » Immobilisation of neck with cervical collar
 - » Suction maybe requires clearing airway - blood/vomit
 - » If the GCS is 8 or less, or is rapidly deteriorating - intubation
 - » Check SpO₂ & Give high flow O₂ as appropriate, consider intubation of patient. **HIGH FLOW O₂** if patient presents with Pneumocephalus
- Establish large-bore intravenous (IV) access.
- Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂ x 1-2 hourly
- Obtained investigations: CBC, Urea, Creatinine, Electrolytes, LFTs, PT APTT & INR and blood glucose/RBS.
- IV fluids therapy: 0.9% NS OR Ringer lactate (R/L) x 1L and 0.9% N.S x 1L x IV x BD/TDS. Recommended maintenance fluids around 30-35ml/kg/day for adults. Adjust fluid therapy based on individual patient factors such as age, comorbidities (e.g., CHF, renal impairment), & hemodynamic status.
- Active bleeding: Cross matching with Arrange 2 units/Pint of PCVs
- Consider Inj. Haemaccel 500ml x IV x SOS (hypotension/shock)
- With vomiting - consider ONE of the following anti-emetics:
 - ↳ Inj. Metoclopramide 10mg/2ml (Metaclo, Maxolon) x IV x TDS
 - ↳ OR Inj. Dimenhydrinate 50mg/ml (Gravinate) x IV x TDS
 - ↳ OR Inj. Ondansetron 8mg/4ml (Onset, Onseron) x diluted in 50-100 ml of 0.9% NS OR D5%W, IV over 15 min.
- Gastroprotective: Inj. Omeprazole 40mg (Risek, Ruling) diluted in 100ml 0.9% NS x IV x OD
- Antibiotic prophylaxis: Inj. Ceftriaxone 2g (Oxidil, Rocephin) x IV x OD
- Management of elevated intracranial pressure (ICP)
- With seizures: Inj. Diazepam 10mg/2ml (Valium) diluted in 8ml 0.9% NS x at dose 5-10mg (5-10ml) IV, may repeat if required. If unresponsive then treat it as status epilepticus (see status epilepticus). **For seizures prophylaxis:** Inj. Levetiracetam 500mg/5ml (Lerace, Epilapsa) at dose 1-2g in 100ml 0.9% NS x IV over 15 min
- Pain control/analgesia: Inj. Paracetamol 1g/100ml (Provas, Paracet) x IV x TDS/SOS. OR Inj. Ketorolac 30mg/1ml (Toradol) in 4-8ml 0.9% N/S x IV
- Neuroprotective: Inj. Alphacholine (Neurocholine) 500mg-1g x IV x BD
- Examine carefully for lacerations, evidence of facial fractures, or depressed skull fractures. Ensure to check for signs of basal skull fractures such as bruising around eyes ('raccoon eyes'), bruising behind the ears (Battle's sign), clear discharge from nose or ear (CSF rhinorrhoea or CSF otorrhoea), blood bulging from middle ear (haemotympanum), or any obvious penetrating injury.

Intraparenchymal

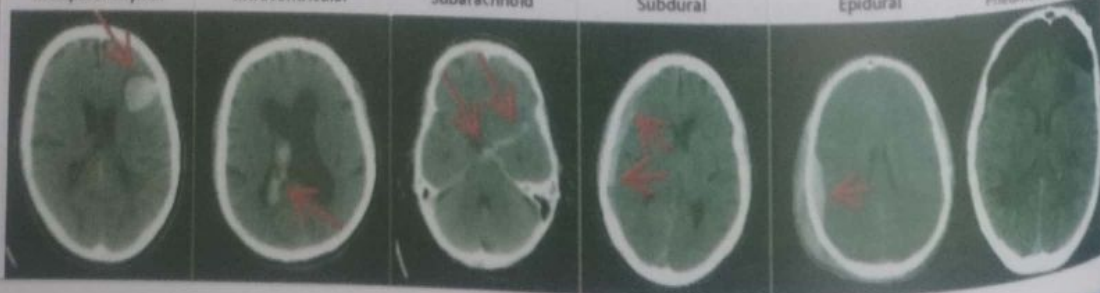
Intraventricular

Subarachnoid

Subdural

Epidural

Pneumocephalus



PNEUMOCEPHALUS (INTRACRANIAL AEROCELE)

Introduction

- Also known as pneumatocele or intracranial aerocele) is defined as the presence of air in the epidural, subdural, or subarachnoid space within the brain parenchyma or ventricular cavities.
- It can occur following trauma (MC), cranial surgeries, or spontaneously
- It is classified as simple or tension pneumocephalus. It can also be classified as acute (< 72 hours) or delayed (72 hours or more).

Presentation

- Headache
- Nausea and Vomiting
- Seizures
- Dizziness
- Obtundation
- An intracranial succession splash is a rare (Occurring = 7%) but pathognomic finding
- Focal deficit and/or increased ICP (features of mass) is seen with tension Pneumocephalus

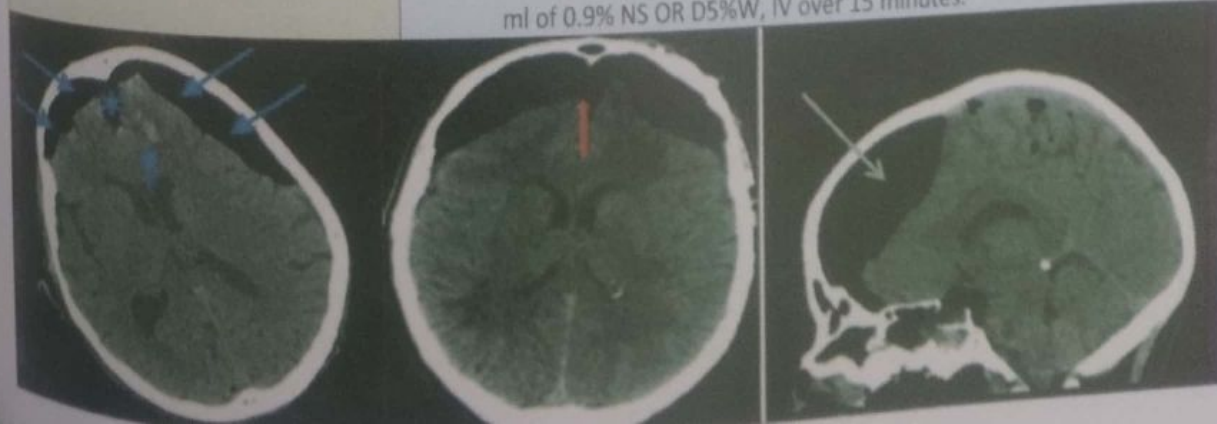
Best initial test: CT Scan brain

Tension pneumocephalus producing significant symptoms must be evacuated. The urgency is similar to that of an intracranial hematoma.

Dramatic and rapid improvement may occur with the release of gas under pressure: placement of new twist drill or burr holes, or insertion of a spinal needle through a pre-existing burr hole (e.g. following a craniotomy).

Rx

- Stabilize patients using ABCD&E approach.
 - Check SpO₂ & Give **HIGH FLOW O₂** via a nonrebreather mask increases the rate of resorption (100% O₂ FiO₂ can be tolerated for 24-48 hours without serious pulmonary toxicity)
 - Consider intubation of patient.
- Establish large-bore intravenous (IV) access.
- Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂.
- Obtained investigations: CBC, BUN, Creatinine, Electrolytes, LFTs, RBS
- IV fluids therapy: 0.9%NS OR Ringer lactate (R/L) x 1L and 0.9% N.S x 1L x IV x BD/TDS. Recommended maintenance fluids around 30-35ml/kg/day for adults. Adjust fluid therapy based on individual patient factors such as age, comorbidities (e.g., heart failure, renal impairment), and hemodynamic status.
- Controlling Elevated intracranial hypertension (ICP): Treat by elevating head-end of the bed to 30°, starting hypertonic saline or mannitol, and hyperventilating the patient. **Mannitol infusion 20%/500ml** (=100 grams) x **Initial dose:** 0.25–1.5 g/kg IV as a single dose (for 70 kg patients' weight, the initial dose = 87.5–525ml) over 30 to 60 minutes, with effects usually seen within 5 to 10 minutes and lasting up to about 6 hours. **Maintenance dose:** 0.25-0.5 g/kg IV every 6 hours or as needed. **Dosage:** should be adjusted according to the patient's age, body weight, and renal function.
- Gastroprotective: Inj. Omeprazole 40mg (Ruling, Risek) diluted in 100ml 0.9% NS x IV x OD
- Antibiotic prophylaxis: Inj. Ceftriaxone 2g (Oxidil, Rocephin) x IV x OD
- With seizures: Inj. Diazepam 10mg/2ml (Valium) diluted in 8ml 0.9% NS x at dose 5-10mg (5-10ml) IV, may repeat if required. If unresponsive then treat it as status epilepticus (see status epilepticus). **For seizures prophylaxis:** Inj. Levetiracetam 500mg/5ml (Lerace, Epilapsa) at dose 1-2g in 100ml 0.9% NS x IV over 15-20 min
- With fever/pain: Inj. Paracetamol 1g/100ml (Provas) x IV x TDS/SOS OR PO Tab. Panadol 500-1000mg x TDS/QID
- With vomiting – consider ONE of the following anti-emetics:
 - Inj. Metoclopramide 10mg/2ml (Metaclo, Maxolon) x IV x TDS
 - OR Inj. Dimenhydrinate 50mg/ml (Gravinate) x IV x TDS
 - OR Inj. Ondansetron 8mg/4ml (Onset, Onseron) x diluted in 50-100 ml of 0.9% NS OR D5%W, IV over 15 minutes.





FEVER WITH DRY COUGH (ACUTE) IN PREGNANCY

△ Upper RTI

C/C:

- » Cough (Dry)
- » Sore throat
- » Runny nose
- » Nasal congestion
- » Headache
- » Low-grade fever
- » Facial pressure
- » sneezing

Duration of treatment: 3-5 days

Dry coughs are usually caused by viral infections, allergies, asthma, irritants, or other non-bacterial factors. Antibiotics are not effective against viruses or non-infectious causes and are generally not recommended for treating dry coughs unless there is a clear bacterial infection.

Rx

1. **General:**
 - » Steam inhalation
 - » Ginger tea
 - » Honey with warm water
2. **Antibiotics (If indicated)** Cap. Ampicillin 500mg (Penbritin)
OR Tab. Co-Amoxiclave 625mg
1-1-1 (TDS)
OR Tab. Azithromycin 500mg (Azomax, Zetro)
0-0-1 (OD)
3. **Syp. Diphenhydramine** (Benadryl)
OR Syp. Coferb
OR Syp. Olcuf
2 Teaspoonful 2 or 3 times a day for 5 days
4. **With fever:** Tab. Paracetamol 500mg (Panadol, Calpol, Febrol)
1-1-1



FEVER WITH PRODUCTIVE COUGH (ACUTE) IN PREGNANCY

△ Lower RTI

C/C:

- » Fever
- » Cough with Sputum production
- » Postnasal drip
- » Rapid breathing or difficulty breathing.
- » Wheezing
- » Skin turning a blue color due to lack of oxygen.
- » Chest pain or tightness

Diagnostic workup

- » CBC
- » ESR
- » Serum electrolytes
- » Sputum culture & gram staining

Duration of treatment: 5-7 days

Rx

1. **Tab. Co-Amoxiclave 625mg** (Augmentin, Calamox)
1-1-1 (TDS)
OR Cap. Cefaclor 500mg (Cefalor, Ceclor)
1-0-1 (BD)
OR Tab. Azithromycin 500mg (Azomax, Zetro)
OR Cap. Cefixime 400mg (Cefim, Cefspan, Cefiget)
0-0-1 (OD)
2. **Tab. Loratidine 10mg** (Softin, Lorin NSA, Loril)
0-0-1 (OD)
3. **With fever:** Tab. Paracetamol (Panadol, Calpol, Febrol)
1-1-1 (TDS) or 2-2-2 (TDS) (at dose 500mg-1000mg (1-2 tablets) x 3-4 times per day. **Maximum:** 4g/day)
4. **Syp. Diphenhydramine** (Benadryl)
OR Syp. Coferb
OR Syp. Olcuf
2 Teaspoonful 2 or 3 times a day for 5 days



TYPHOID FEVER (ENTERIC FEVER) IN PREGNANCY

Typhoid fever, also known as **Enteric fever**, is a systemic infection caused primarily by *Salmonella enterica* serotype Typhi and sometimes by *Salmonella enterica* serotype Paratyphi. The condition poses significant risks to both the pregnant woman and the fetus, necessitating careful management.

- ☞ **Transmission:** fecal-oral → **Direct:** person-to-person contact from contaminated stool via handshake to the next person and **Indirect:** contaminated food and water.
- ☞ **Incubation period:** 5–30 days (most commonly 7–14 days)
- ☞ If left untreated, three different disease stages, each lasting a week, classically occur.
- ☞ **After 3 weeks of disease:** slow regression of symptoms; patients may become chronic salmonella carriers

Clinical features

- » Fever low then gradually increases to 104.9°F
- » Headache
- » Vomiting
- » Weakness and fatigue
- » Muscle aches
- » Relative bradycardia
- » Loss of appetite
- » Abdominal pain
- » Rash (Rose spot)
- » Diarrhea
- » Hepatosplenomegaly

Diagnostic workup

- » **Most accurate test:** Blood culture is the most important diagnostic test at disease onset, as stool cultures are often **-ve** despite active infection. Blood culture, which is **+ve** in the 1st week of illness in 80% of patients who have not taken antibiotics therapy.
- » **CBC:** Anemia, Thrombocytopenia, Leukopenia or leukocytosis
- » **LFTs:** maybe abnormal (Transaminitis)
- » **Ultrasound abdomen:** Hepatosplenomegaly.
- » **Gold standard:** Bone marrow culture occasionally **+ve** but rarely performed

Definitive treatment: *Salmonella* bacterial may sequester in the gallbladder.

Cholecystectomy may be required if prolonged antibiotics therapy fails.

Rx

1. **Hydration:** Ensure adequate fluid intake to prevent dehydration.
2. **Cap. Cefixime 400mg** (Cefspan, Cefiget, Cefim) x BD
Dose: 20mg/kg, twice daily for 10-14 days.
OR **Tab. Azithromycin 500mg** (Azomax, Azitma) x 1g (2 tablets) once daily (OD) then 500mg OD for 7 days
3. **Fever/pain relief:** **Tab. Paracetamol 500mg** (Calpol, Panadol) 1-1-1 (TDS) or 2-2-2 (TDS) {at dose 500mg – 1000mg (1-2 tablets) x 3-4 times per day. **Maximum: 4g/day}**
4. **Syp. Lysovit OR Syp. Leaderplex**
2-0-2 (2 teaspoonful x two times a day)

With Epigastric upset

5. **Tab. Pantoprazole 40mg** (Zopent)
0-0-1 (OD) 30 منٹ پہلے سے کھاتے

With Nausea/vomiting

6. **Tab. Metoclopramide 10mg** (Metaclon, Maxolon) 1-1-1 (TDS)
OR **Tab. Ondansetron 4mg** (Onset, Onseron) x BD/TDS 1-0-1 (BD) OR 1-1-1 (TDS)
30 منٹ پہلے سے کھاتے

Rx

FOR SEVERE TYPHOID FEVER (ENTERIC FEVER)

- ☞ **Consider hospitalization**
- ☞ Regular monitoring of maternal and fetal well-being.
- ☞ **Inj. Ceftriaxone 2g** (Oxidil, Rocephin, Titan) x IV x OD
 - » Dose: 50-60mg/kg
 - » Dilution: Diluted in 100ml 0.9% N/S
- ☞ **Fever:** **Inj. Paracetamol 1g/100ml** (Provas) x 8 hourly or SOS
- ☞ **Vomiting:** **Inj. Metoclopramide 10mg/2ml** (Metaclon) x IV x TDS
- ☞ **Correct dehydration and electrolytes imbalance**

Prevention

Salmonella infection is best prevented by protecting the water supply, preventing fecal contamination during food production, cooking and refrigerating foods, pasteurizing milk and milk products, and handwashing before preparing foods.

MALARIA FEVER (FALCIPARUM MALARIA) IN PREGNANCY



Clinical features

Symptoms

- » Fever with chill and rigor
- » Headache/Body ache
- » Sweats, Fatigue, general malaise
- » Nausea, vomiting and Diarrhea
- » General malaise
- » Cough, Dyspnea
- » Muscle or back pain
- » Loss of appetite

Signs

- » Increase temperature
- » Sweating
- » Pallor
- » Jaundice
- » Respiratory distress
- » Splenomegaly

Diagnostic workup

- » Microscopy of thick and thin blood films (gold standard test for peripheral blood for malaria).
- » In pregnant women, placental histology is the gold standard for diagnosis of malaria
- » Malaria parasite Rapid detection tests (Low sensitivity)
- » **Routine test:** CBC, LFTs, RBS, BUN, RFT, S/electrolytes, serum Lactate and ABGs
- » Urine D/R
- » Blood/Urine C/S



Uncomplicated malaria (First trimester treatment)

- » Treat malaria in pregnancy as an emergency
- » Admit pregnant women with uncomplicated malaria to hospital and pregnant women with severe and complicated malaria to an intensive care unit.
- 1. **Tab Quinine 300mg x TDS PLUS Cap. Clindamycin 300mg x TDS for 7 days**
OR Inj. Quinine 10mg/kg (Diluted) x BD PLUS Clindamycin 5mg/kg x BD
Alternative: (Artem DS Plus, Artheget DS Plus, Gen-M 80/480mg)
Tab. Artemether 80 + Lumefantrine 480mg
1-0-1 (BD) for 3 days
- 2. **Tab. Paracetamol** (Panadol, Calpol, Febrol)
1-1-1 (TDS), increase if not repond or adv cold sponging
- 3. **Syp. Multivitamins** (Lysovit, Leaderplex)
2-0-2 (2 teaspoonful twice daily)



Complicated Severe malaria

Preferred treatment for Severe malaria in All trimesters

- » **Inj. Artesunate 30mg, 60mg or 120mg** (Gen-M) x IV or IM at dose 2.4 mg/kg at 0, 12, 24 hours, and daily thereafter
(see Falciparum Malaria in ER section for IV dilution or follow GEN-M leaflet info)
- » Treat for at least 24hrs, or until able to tolerate oral medication
- » Complete treatment with 3 days of Artemisinin based combined therapy (ACT)
= **Artemether + Lumefantrine (Artem DS Plus) x BD**

If Artesunate is not available:

- » **Inj. Artemether 40mg/ml or 80mg/ml** (Artem) at dosage of 3.2 mg/kg as loading dose, followed by 1.6 mg/kg daily until able to tolerate oral drugs
- » Complete treatment with three days of artemisinin-based combined therapy (ACT) = **Artemether + Lumefantrine**
- » **Treat fever with Inj. Paracetamol 1g/100ml** (Provas) x IV x TDS
- » **Correction of hypoglycemia**

WHO recommendations to avoid artemisinin-based combined therapy (ACT) in the first trimester were updated in 2015, following updated evidence showing no increase in the risk of miscarriage, stillbirths, or major congenital malformations compared to quinine. **Most of the evidence relates to (Artemether + Lumefantrine), therefore this should be the preferred ACT.**

Reference: WHO Evidence Review Group. Malaria in pregnancy. Malaria Policy Advisory Committee Meeting. September 2015. Available at: <http://www.who.int/malaria/mpac/mpac-sept2015-erg-mip-report.pdf>. Last accessed 30 July 2017.

Oxford textbook of medicine 6th international edition, Section 14, page no 2675, 2676

Clinical and laboratory features of severe malaria

Clinical features	Laboratory features
» Impaired consciousness: GSC <11	» Hypoglycaemia: (<2.2 mmol/litre or <40 mg/dl)
» Prostration: generalized weakness, unable to sit, stand, or walk without assistance	» Pulmonary oedema: radiological diagnosis
» Multiple convulsions: >2 episodes within 24 hr.	» Metabolic acidosis: plasma Bicarb <15 mmol/litre
» Respiratory distress: (acidotic breathing or respiratory rate >30 breaths/min)	» Hyperlactataemia: lactate > 5 mmol/l
» Hypotension (systolic BP <80 mm Hg)	» Acute kidney injury: serum creatinine more than 265 µmol/l or blood urea more than 20 mmol/l
» Jaundice	» Severe anaemia: Hb < 7 g/dl, or PCV <20%
» Abnormal bleeding	» Jaundice: bilirubin more than 50 µmol/l (3 mg/dl)
	» Hyperparasitaemia: more than 4% parasitaemia



URINARY TRACT INFECTION (UTI) IN PREGNANCY

Causes:

- » Bacterial infection, commonly caused by *Escherichia coli* (E. coli).
- » Less commonly caused by other bacteria like *Klebsiella*, *Proteus*, and *Staphylococcus saprophyticus*.

Risk Factors:

- » Hormonal changes that relax the urinary tract muscles, slowing urine flow.
- » Enlarged uterus putting pressure on the bladder, causing incomplete emptying.
- » Increased glucose levels in urine during pregnancy.
- » Sexual activity.
- » History of UTIs.

Clinical features

- » Mild fever $\pm$ with chills, malaise
- » Burning micturition
- » Abdominal (Suprapubic) pain
- » Painful urination (Dysuria)
- » Frequent urination but very little urine comes out
- » Urgent urination

Diagnostic workup:

- » **Urinalysis:** Detects the presence of leukocytes, nitrites, and bacteria.
- » **Urine Culture:** Identifies the specific bacteria causing the infection and their antibiotic sensitivities.



TREATMENT OF UTI IN PREGNANCY

1. General Measures:

- » **Hydration:** Increase fluid intake to help flush out bacteria. Drinking plenty of water is crucial.
- » Encourage frequent urination to prevent bacterial growth and promote flushing of the urinary tract.
- » **Hygiene:** Advise proper hygiene practices, including wiping from front to back and avoiding irritants like douches and certain soaps.
- » **Avoidance of Irritants:** Reduce consumption of caffeinated and carbonated drinks, which may irritate the bladder.

2. Fosfomycin 3g sachets (FOCIN) orally, as a single dose.

OR Tab. Co-Amoxiclav 625mg (Augmentin, Calamox) x BD/TDS

OR Cap. Cephalexin 500mg (Keflex, Ceporex) x BD/TDS

OR Cap. Cefaclor 500mg (Ceclor, Cefalor) x BD

3. Tab. Paracetamol 500mg (Panadol, Calpol)

1-1-1 (TDS), at dose 500-1000mg orally three times daily (TDS).

4. Cranberry extract sachets (Cranmax pro, Abocran)

One sachet in a glass water x BD

Antibiotics that are potentially appropriate during specific stages of pregnancy include:

- » Tab. Nitrofurantoin 100mg x BD for 5 days: Avoid close to the delivery date. Women with G6PD deficiency should avoid Nitrofurantoin (also should avoided in 3rd Trimester - Risk of neonatal hemolysis)
- » Tab. Septran DS x BD for 3 days: Avoid during the first trimester and past 32 weeks' gestation.

Antibiotics that should be avoided include fluoroquinolones and aminoglycosides.

Follow-up culture should be considered a week after treatment for UTI.

- » **Negative culture:** no further treatment required unless new UTI symptoms develop
- » **Positive culture:** indicates persistent bacteriuria; antibiotic therapy based on the culture results

NEPHROLITHIASIS (RENAL STONES) IN PREGNANCY

△ Nephrolithiasis in Pregnancy

- C/C:
- » Tiny renal stone <8 mm in size
 - » Sudden onset of severe U/L and colicky flank pain (renal colic)
 - » Radiates anteriorly to the lower abdomen, groin, labia, testicles, or perineum
 - » Nausea vomiting
 - » Hematuria
 - » Dysuria, frequency, and urgency
 - » Passage of gravel or a stone

Diagnostic workup

- » CBC – WBCs increases
- » Serum Urea, creatinine & Electrolyte
- » Uric acid, Calcium & phosphorus level
- » Urine D/R & Urine C/S
- » Ultrasound KUB
- » Low-dose CT scan or MRI KUB

Low-dose CT and MRI are more informative and comparatively safer in pregnancy, while **conventional high-dose CT scan is contraindicated.**



Conservative treatment of Nephrolithiasis

Antibiotics indicated in case of concomitant UTI

1. Cap. Amoxicillin 500mg (Amoxil, Zeemox) x TDS
OR Tab. Co-Amoxiclav 625mg (Augmentin) x TDS
OR Cap. Cephalexin 500mg (Ceporex, Keflex) x BD
OR Cap. Cefixime 400mg (Cefspan, Cefiget)
0 – 0 – 1 (OD)

2. Tab. Paracetamol (Panadol, Calpol)
1 – 1 – 1 (TDS)

For spasm/colicky pain

3. Tab. Phenazopyridine 100mg (Urilef, Uropin) x BD (Category-B)
OR Tab. Drotaverine 80mg (Relispa forte, Nospa forte)
1 – 0 – 1 (BD)

Expulsive therapy can reduce ureteral spasm and increase spontaneous passage rates by about 50%.

4. Cap. Tamsulosin 0.4mg (Tamsolin, Maxflow, Prostreat)
0 – 0 – 1 (OD) (Category-B)

5. **Adequate Oral Hydration:** Increase oral fluid intake

Medical Expulsive Therapy: Kidney stones 5 mm or smaller have about a 70% probability of passing spontaneously, whereas stones between 5 and 7 mm have a 60% chance, stones 7 to 9 mm have a 48% chance, and stones 9 mm or larger have a 25% chance of passing spontaneously. Stones located more distally in the ureter are more likely to pass spontaneously. Medical expulsive therapy may be cautiously attempted with ureteral stones smaller than 10 mm diameter for 4 to 6 weeks if pain is controlled, kidney function is normal, and there is no evidence of urinary tract infection or significant obstruction. The patient must be followed closely, generally with repeat ultrasound examinations every week or 2 weeks.

Overview - Types of Stone

Stone Type	Incidence	Etiology
» Calcium Oxalate	~75%	» Hypercalciuria » Hyperoxaluria » Hypocitraturia » ↓ Urine pH
» Uric acid	~10%	» ↓ Urine pH » Hyperuricemia/Gout » Hyperuricosuria
» Struvite	~5-10%	» UTI with urease-producing bacteria
» Calcium phosphate	<5%	» Hyperparathyroidism » Type-I RTA (Renal Artery Stenosis)
» Cysteine	<5%	» Cystinuria



PNEUMONIA OUTPATIENT (OPD) TREATMENT IN PREGNANCY

Clinical features

- ☛ **Typical pneumonia:** It is characterized by a sudden onset of symptoms caused by lobar infiltration.
 - » Severe malaise
 - » High fever and chills
 - » Productive cough with purulent sputum (yellow-greenish)
 - Crackles and bronchial breath sound on auscultation
 - Decreased breath sounds
 - Enhanced bronchophony, egophony, and tactile fremitus
 - » Dullness on percussion
 - » Tachypnea and dyspnea (nasal flaring, thoracic retractions)
 - » Pleuritic chest pain when breathing, often accompanying pleural effusion
 - » Pain that radiates to the abdomen and epigastric region (particularly in children).
- ☛ **Atypical pneumonia:** typically, has an indolent course (slow onset) and commonly manifests with extrapulmonary symptoms.
 - » Nonproductive, dry cough
 - » Dyspnea
 - » Auscultation often unremarkable
 - » **Common extrapulmonary features** include fatigue, headaches, sore throat, myalgias, and malaise

Diagnostic workup

- ☛ **Diagnosis:** Pneumonia is a clinical diagnosis based on history, physical examination, laboratory findings, and imaging findings. Consider microbiological studies and advanced diagnostics based on patient history, comorbidities, severity, and entity of pneumonia.
- ☛ **Laboratory findings:**
 - » **CBC:** Leukocytosis or leukopenia,
 - » **Inflammatory markers:** ↑ CRP, ↑ ESR
 - » **Sputum Culture:** If productive cough is present, to identify the causative organism.
 - » **Nasal Swabs:** For viral pathogens, particularly in flu season.
 - » **Serum procalcitonin (PCT):** ↑, PCT is an acute phase reactant that can help to diagnose bacterial lower respiratory tract infection.
 - » **Blood Cultures:** To identify causative bacteria, though often negative.



PNEUMONIA OPD TREATMENT IN PREGNANCY

Previously healthy patients without comorbidities or risk factors for resistant pathogens

- ☛ **Cap. Amoxicillin 500mg x 2 (Amoxil) 1g x Three time daily (TDS)**
OR **Tab. Azithromycin 500mg (Azomax) x 500mg on day-1,**
followed by 250mg once daily for 4 days or 500mg OD for 3 days.
OR **Cap. Cefixime 400mg (Cefspan, Cefim, Cefiget) x OD**

Patients with comorbidities or risk factors for resistant pathogens

Combination therapy

- » **Tab. Amoxicillin/clavulanic acid 1g (Augmentin) x BD**
OR **Cap. Cefuroxime 250mg (Zinacef, Zecef) x 500mg x BD**
OR **Tab. Cefpodoxime 200mg (Prelox, Orelox) x BD**

PLUS, One of the following:

- » **Tab. Azithromycin 500mg (Azomax) x 500mg on day-1,**
followed by 250mg OD for 4 days or 500mg OD for 3 days.

Supportive treatment

- » **Ensure adequate hydration, nutrition, and rest**
- » **Fever:** Tab. Paracetamol 500mg (Panadol) x 1-2 tablets x TDS
- » **Calcium/vitamins supplement:** Abocal or CAC-1000 x OD
- » **Antihistamine:** Tab. Loratidine 10mg x OD

PNEUMONIA INPATIENT (WARD) TREATMENT IN PREGNANCY



1. Airway:

- » Ensure patient is maintaining own airway
- » Assess and secure stable airway

2. Breathing: Check SpO₂ if <94 administer O₂ therapy via nasal canula: 1-6 L O₂/minutes

3. Circulation:

- » Maintain 2 large bore intravenous line (IV cannula)
- » Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂
- » Send labs: CBC, UCE, LFTs, PT, INR, LDH, CRP, ESR, RBS, Cardiac Enzyme, Procalcitonin, D-dimer.
- » Hydration with PO fluids or IV fluids: Ringer Lactate or 0.9% Normal saline x 1L x IV x stat
- » Empiric antibiotic therapy for community-acquired pneumonia

» Duration of therapy 5-7 days is usually sufficient.

Combination therapy for Non-ICU/non-severe & ICU/severe patients

- Inj. Ampicillin-Sulbactam 1.5-3g (Ambac) x IV x QID (every 6 hours)
- OR Inj. Amoxicillin-Sulbactam 1.5-3g (Bactamox) x IV x QID (every 6 hours)
- OR Inj. Ceftriaxone 1-2g (Oxidil, Titan, Rocephin) x IV x BD/OD (every 12-24 hours)
- OR Inj. Cefotaxime 1-2g (Claforan, Cefotax) x IV x TDS/BD (every 8-12 hours)

PLUS, One of the following:

- Inj. Azithromycin 500mg/vial (Azitma, Zerot) x IV x OD (can also be given orally in tablet form)

» Empiric antibiotic therapy for Risk factors for *Pseudomonas aeruginosa***Combination therapy**

- Inj. Piperacillin + Tazobactam 4.5g (Tanzo, Tazocin EF) x IV x QID (every 6 hours)
- OR Inj. Ceftazidime 1-2g (Fortum) x IV x (every 8 hours)
- OR Inj. Cefepime 1-2g (Uceph) x IV x TDS (every 8 hours)
- OR Inj. Meropenem 1g (Meronem, Penro) x IV x TDS (every 8 hours)
- OR Inj. Imipenem-cilastatin 500mg-1g (Cilapen, Tienam) x IV x QID (every 6 hours)

PLUS one of the following:

- Inj. Azithromycin 500mg/vial (Azitma, Zerot) x IV x OD
- » If indicated Corticosteroids: (Corticosteroids are not routinely recommended as adjunct therapy).
- Inj Dexamethasone 4mg/1ml (Decadron) 4-6mg x IV x BD for 5-7 days
- » Fever: Inj. Paracetamol 1g/100ml (Provas) x IV x TDS
- » Gastroprotective: Inj. Pantoprazole 40mg (Zopent) x IV x OD
- » Thromboprophylaxis (high risk patient)
- Inj Enoxaparin sodium 40mg (Clexane) x SC x OD

4. Disability & Exposure

- » Admit to ICU and initiate intubation if any of the following are present: Signs of respiratory failure, Dyspnea with hypoxemia and Tachypnea (RR > 30/min)
- » Monitor pupillary reflexes and GCS level
- » Supportive care: Adequate hydration, nutrition, and rest
- » Correct underlying cause



CHRONIC HEPATITIS B VIRAL (HBV) INFECTION IN PREGNANCY

△ Chronic HBV Infection

C/C:

- » Most patients are inactive, non-contagious carriers.
- » Potential reactivation of chronic inactive hepatitis can manifest variably in the following ways:
 - » Asymptomatic
 - » Unspecific symptoms
 - ⊗ Fatigue, malaise
 - ⊗ Nausea, poor appetite
 - ⊗ Unspecific abdominal pain
 - ⊗ Similar to acute hepatitis
 - ⊗ Hepatic failure

Diagnostic workup

Specific Investigation

- » Screening: measure HBsAg and anti-HBc IgM
- » If HBsAg is positive: measure HBeAg and HBV DNA to determine transmissibility.

Routine investigation

- » CBC may show anemia
- » LFTs, Albumin, ChE, PT & INR
 - ⊗ Chronic hepatitis
 - High variability: mildly ↑ or unchanged AST & ALT
 - AST/ALT ratio ≥ 1
 - GGT: ↑
 - ⊗ Cirrhosis
 - Albumin: ↓
 - INR/PT: ↑
 - Bilirubin: ↑
 - Serum cholinesterase (ChE): ↓

N.B: Serum ChE is an excellent biomarker of cirrhosis with good sensitivity and specificity. It shows good correlation with serum albumin, PT INR and MELD score. Since it distinguishes

Decompensated cirrhosis from compensated cirrhosis well, low levels in cirrhosis may serve as a useful prognostic marker of advanced liver disease.

Test of common coinfections: Coinfection with hepatitis C, hepatitis D, syphilis, and HIV is common and should be tested for accordingly.

Ultrasound abdomen:

- » Decreases Echogenicity and number of portal vein radicle walls
- » Increases Liver echogenicity

Duration: 48 weeks or more



TREATMENT OF CHRONIC HBV INFECTION

Lifestyle changes

- » Weight loss
- » Cessation of substance use (including alcohol)
- » Discontinuation of hepatotoxic medication.

(Tenofo-B, Hilfovir, Gentovir, Vireof)

1. Tab. Tenofovir Disoproxil Fumarate 300mg

OR Tab. Lamivudine 100mg (Zeffix)

OR Tab. Telbivudine 600mg (Sebivo)

0-0-1 (OD)

Timing: Antiviral therapy is typically started in the third trimester to reduce viral load and lower the risk of transmission to the infant.

Indications of Antiviral Therapy:

- » High HBV viral load ($>200,000$ IU/mL) during pregnancy.
- » Elevated liver enzymes or signs of liver inflammation.
- » History of severe liver disease.

2. Tab. L-Methylefolate 400mcg (Myfol, Maxfol, Folate)

0-0-1 (OD)

With constipation

3. Syp. Lactulose (Duphalac, Lilac)

0-0-20-30ml x HS

4. Cap. Esomeprazole 40mg (Eskem, Nexum, Esso)

OR Cap. Omeprazole 40mg (Omega, Risek, Ruling)

0-0-1 (OD)

کھانے سے 30 منٹ پہلے

» **Hepatitis B in pregnancy:** Tenofovir (DOC), Lamivudine, & Telbivudine (PEG-IFN- α is contraindicated during pregnancy)

» Liver biopsy

Biopsy is indicated in the following cases:

- » Diagnosis is uncertain.
- » Exclusion of other possible causes of liver damage in chronic disease or severely affected individuals
- » Assessment of disease severity in patients with active chronic liver disease (i.e., $\uparrow$ AST/ALT and detectable levels of HBV DNA)

» Liver transplantation

- » In cases of end-stage liver disease due to HBV
- » In cases of fulminant hepatic failure (emergent transplantation)

VAGINAL YEAST INFECTION (VULVO-VAGINAL CANDIDIASIS)



- **Epidemiology:** Second most common cause of vulvovaginitis (17–39% of all cases)
- **Pathogen:** primarily *Candida albicans* (In immunosuppressed patients also *Candida glabrata*)
- **Pathophysiology:** overgrowth of *C. albicans*.
- **Can be precipitated by the following risk factors:** Pregnancy, Immunodeficiency, Both systemic (Diabetes mellitus, HIV, immunosuppression) and local (Topical corticosteroids) and antimicrobial treatment (after systemic antibiotic treatment)

△ Vaginal Candidiasis

C/C:

- White, crumbly, and sticky vaginal discharge that may appear like cottage cheese and is typically odorless
- Erythematous vulva and vagina
- Vaginal burning sensation, strong pruritus, dysuria, dyspareunia

Diagnostic workup

- Pseudohyphae on wet mount with potassium hydroxide (KOH)
- Vaginal pH within normal range (4–4.5)

Rx

1. **Cap. Fluconazole 150mg** (Diflucan)
0 – 0 – 1 (OD) x single dose, if severe repeat on day 7
2. **Tab Metronidazole 400mg** (Flagyl, Metrozine)
1 – 0 – 1 (BD) for 7 days

For married female only

3. **Clotrimazole Vaginal Cream** (Canesten, Gynosporin)
OR **Miconazole Vaginal Cream** (Gyno-Daktarin, Myzovag)
One applicatorfull Intravaginally for 6 days at night Or twice daily for 3 days OR as per physician instruction

CHLAMYDIAL INFECTIONS IN WOMEN

- **Causative organism:** *Chlamydia trachomatis* (serotype D-K) – obligatory intracellular gram-negative bacteria.
- ONE of the most common STIs and ONE of the most common causes of pelvic inflammatory disease (PID)
- **Mode of transmission (MOT):** Sexual intercourse (may be transmitted through genital-to-genital contact or oropharyngeal-to-genital contact, Vaginal birth (in which the mother is infected)
- **Incubation period:** 6–14 days longer (compared to gonorrhea 3–7 days).

Clinical features

- These are non-specific & asymptomatic in most (75–80%) cases.
- **Presenting symptoms:**
 - Dysuria (urethritis)
 - Dyspareunia
 - Vaginal discharge
 - Postcoital bleeding
 - Intermenstrual bleeding
 - Features of salpingitis, cervicitis & PID
 - Patients may present with sign and symptoms of reactive arthritis
- **On Examination:** yellow mucopurulent cervical discharge, cervical edema, cervical ectopy, and cervical friability.
- **Preferred test:** Nucleic Acid Amplification Test (NAAT)/PCR and culture.
- **Test for common STI coinfections should be done in All patients:** HIV testing, gonorrhea testing, syphilis testing

Rx

TREATMENT OF CHLAMYDIAL INFECTION IN WOMEN

- **When possible, provide the complete regimen and administer the first dose at the time of visit.**
 - **Evaluate and treat sexual partners (offer expedited partner therapy where available):** All partners in the last 60 days OR, if no partners in the past 60 days, the most recent partner
 - **Advice patients to abstain from sexual intercourse until all the following criteria are met:** 1) Completion of a 7-day regimen or for 7 days after a single-dose regimen. 2) Symptom resolution. 3) All sexual partners have completed treatment.
1. **Tab. Azithromycin 500mg** (Azitma, Azomax) x 2 tablets (1g) once OR **Cap. Doxycycline 100mg** (Doxyn, Vibramycin) x BD for 7 days OR **Tab. Levofloxacin 500mg** (Leflox) x OD for 7 days
 2. **Tab. Metronidazole 400mg** (Flagyl, Metrozine) x BD for 7 days
- **Pregnant patients:** **Tab. Azithromycin 500mg** (Azitma, Azomax) x 2 tablets (1g) once OR **Cap. Amoxil 500mg** x TDS for 7 days.



LEUKORRHEA

TYPES OF LEUKORRHEA

1. **Physiologic Leukorrhea:** Leukorrhea is defined strictly as an excessive normal vaginal discharge due to estrogen stimulation, which stains the undergarment. It can be a natural defense mechanism that the vagina uses to maintain its chemical balance, as well as to preserve the flexibility of the vaginal tissue. It is nonpurulent, non-offensive and never causes pruritus. The excess normal secretion occurs during puberty, menstrual cycle (around ovulation and premenstrual), sexual excitement and pregnancy due to increased blood flow to the vagina due to increased estrogen.
 - » Normal vaginal discharge in a reproductive-aged woman, also called physiologic discharge, usually consists of 1-4 mL per 24 hours. It is typically transparent, odorless (but can also be slightly malodorous), mucousy, and white-to-yellowish.
 - » Improvement of general health, sympathetic attitude towards ailments, local hygiene and appropriate therapy for the local ailments are enough to cure the state.
2. **Inflammatory Leukorrhea** (Abnormal vaginal discharge is mainly infective in origin)
 - » It may also result from inflammation or congestion of the vaginal mucosa. In cases where it is yellowish or gives off an odor, a doctor should be consulted since it could be a sign of several disease processes, including an organic bacterial infection (Aerobic vaginitis) or STD.
 - » After delivery, Leukorrhea accompanied by backache and foul-smelling lochia (post-partum vaginal discharge, containing blood, mucus, and placental tissue) may suggest the failure of involution (the uterus returning to pre-pregnancy size) due to infection. A number of investigations such as wet smear, Gram stain, culture, Pap smear and biopsy are suggested to diagnose the condition. It may be caused by sexually transmitted diseases; therefore, treating the STD will help treat the leukorrhea.
3. **Parasitic Leukorrhea:** Leukorrhea is also caused by trichomonads, a group of parasitic protozoans, specifically trichomonas vaginalis. Common symptoms of this disease are burning sensation, itching & discharge of frothy substance, thick, white or yellow mucous.



TREATMENT OF LEUCORRHEA

1. Tab. Metronidazole 400mg (Flagyl, Klint)
1-0-1 (BD)
2. Cap. Doxycycline 100mg (Doxyn, Vibramycin)
OR Cap. Clindamycin 300mg (Delacin-C)
OR Cap. Azithromycin 250mg (Azomax, Zetro)
1-0-1 (BD)

For abdominal/pelvic pain/cramps if present

3. Tab. Diclofenac sodium 50mg (Voren, Voltral) x 1-0-1 (BD)
OR Tab. Diclofenac Potassium 50mg (Caflam, Maxit) x 1-0-1 (BD)
 4. **Vegiwash** – Feminine intimate cleanser x 2-3 time weekly
 - » Intimate wash (Enriched with Lactic acid, Triclosan and tea tree oil) helps balance vaginal pH level, which in turn helps in preventing itchiness and bacterial infection in the vaginal area. It also supports the growth of good bacteria, Lactobacillus, which is important for a healthy vagina.
 - » How to use an intimate wash?
 - » Take a small quantity of the solution in your hand and apply it on the external part of the vaginal area during toilet usage or a shower. Apply it gently & then rinse it with clean water.
 - » Dry the area with a clean towel.
 - » Patient can use the intimate wash 2-3 time a week or everyday but use a gentle product that contains natural ingredients.
- ❖ **Duration of Treatment:** 7 – 10 days.

PELVIC INFLAMMATORY DISEASES (PID)



Risk factors

- Multiple sexual partners, unprotected sex
- History of prior STIs and/or adnexitis
- Intrauterine devices
- Risk is lower during pregnancy; PID development during pregnancy increases the risk of maternal morbidity and preterm births.
- Vaginal dysbiosis

Possible sites of infection

- Cervix: Cervicitis
- Endometrium: Endometritis
- Fallopian tubes: Salpingitis
- Ovaries: Oophoritis
- Uterine adnexa: Adnexitis
- Surrounding pelvic structures (parametritis) or, in some cases, the peritoneum: Peritonitis

△ PID

C/C:

- Fever, chills
- Lower abdominal pain (generally bilateral), which may progress to acute abdomen
- Menstrual disturbance** (Menorrhagia, metrorrhagia)
- Pain during sexual intercourse
- Post coital pain.
- Vaginal odor & itching.
- Abnormal Vaginal discharge (yellow/green color)
- Dysuria, urinary urgency

Microbes involve:

Most common:

- Chlamydia trachomatis 1/3
- Neisseria gonorrhoeae 1/3

Less common (consider coinfections):

- E. coli
- Ureaplasma
- Mycoplasma
- Endogenous aerobes
- Anaerobes

Diagnostic workup:

Blood test: ↑ ESR, Leukocytosis (↑ TLC)

Pregnancy test: To rule out an (Ectopic) pregnancy

Cervical and urethral swab

Gonococcal and chlamydial DNA (PCR) and culture sensitivity.

Giemsa stain of discharge can show cytoplasmic inclusions in Chlamydia trachomatis infections, but not in N. gonorrhoeae infection.



First line treatment (Regimen-A)

- Cap. Doxycycline 100mg (Vibramycin, Doxyn)
1 - 0 - 1 (BD)
- Tab. Metronidazole 400mg (Flagyl, Metrozine)
1 - 0 - 1 (BD)
- Tab. Ciprofloxacin 250mg (Novidat, Ciplet)
1 - 0 - 1 (TDS)
- Cap. Omeprazole 40mg (Ruling, Risek)
0 - 0 - 1 (OD)
کھانے سے 30 منٹ پہلے
- Clindamycin phosphate Vaginal Cream (Vagibact, Clycin-V)
0 - 0 - 1 (HS)



Regimen-B

- Tab. Levofloxacin 500mg (Leflox, Levofin, Levoxin) x 14 days
OR Tab. Azithromycin 250mg (Azomax, Zetro) x 7-10 days
0 - 0 - 1 (OD)
- Tab. Metronidazole 400mg (Flagyl, Metrozine)
1 - 0 - 1 (BD)
- Cap. Esomeprazole 40mg (Esso, Nexum)
0 - 0 - 1 (OD)
کھانے سے 30 منٹ پہلے
- Clindamycin phosphate Vaginal Cream (Vagibact, Clycin-V)
0 - 0 - 1 (HS)



Ultrasound pelvic: Bulky uterus, free fluid in cul de sac, abscesses, tuboovarian cyst, pyosalpinx/hydrosalpinx.

IMPORTANT DIAGNOSTIC CRITERIA FOR PID

- » **Patient history:** Most often a sexually active young woman
- » Lower abdominal pain
- » **Vaginal examination**
 - ↳ Chandelier sign (Cervical motion tenderness): severe cervical pain elicited by pelvic examination
 - ↳ Uterine and/or adnexal tenderness
 - ↳ Purulent, bloody cervical and/or vaginal discharge

Duration of treatment: 14 days

Rx

Regimen-C

1. Inj. Ceftriaxone 2 g (Oxidil, Titan), diluted in 100ml 0.9% normal saline x IV x Once in hospital/clinic setup.
2. Cap. Doxycycline 100mg (Vibramycin, Doxyn) 1-0-1 (BD)
3. Tab. Metronidazole 400mg (Flagyl, Klint) 1-0-1 (BD)
4. Clindamycin phosphate Vaginal Cream (Vagibact, Clycin-V) 0-0-1 (HS)

Rx

SURGICAL TREATMENT

- » If mass persist OR Abscess is > 4-6 cm
↓
Drainage of a Tubo-ovarian/Pelvic abscess is appropriate
- » Mass in cul-de sac in midline, Drain through the vagina
↓
If patient condition deteriorates
↓
LAPROSCOPY OR LAPROTOMY

VAGINAL TRICHOMONIASIS

- » Vaginal trichomoniasis is the most common and important cause of vaginitis in the childbearing period.
- » **Pathogen:** Trichomonas vaginalis a pear-shaped unicellular flagellate and motile anaerobic protozoa.
- » **Mode of Transmission:** Predominantly transmitted by sexual contact, the male harbors the infection in the urethra and prostate. It is a highly contagious STI. The incubation period is 3-28 days.

Clinical features

- » Pelvic pain
- » Sudden profuse, foul-smelling, frothy, yellow-green vaginal discharge often dating from the last menstruation.
- » Irritation and itching of varying degrees within & around the introitus are common.
- » Burning sensation
- » **Urinary symptoms:** Dysuria and frequency of micturition.
- » Strawberry cervix (erythematous mucosa with petechiae)
- » **Dyspareunia:** Painful intercourse

Diagnostic workup

- » **Saline wet mount of vaginal smear:** motile trophozoites with multiple flagella.
- » If wet mount is inconclusive, perform culture
- » pH of vaginal discharge > 4.5
- » **NAATs** are 3-5 times more sensitive than wet preparation. NAAT can be done with vaginal discharge or urine

Rx

TREATMENT OF VAGINAL TRICHOMONIASIS

- » Consider oral metronidazole OR tinidazole for the patient and sexual partners and Check for other STIs
- » Metronidazole is safe in all trimesters of pregnancy (DC Dutta)
- » The husband should use condom during coitus irrespective of contraceptive practice until the wife is cured.
 - ↳ **Tab. Metronidazole 400mg** (Flagyl, Klint) 1-0-1 (BD) for 7 days, OR single dose 2 g x Once
 - Recommended regimen:** Tab. Metronidazole 2g per oral by single dose OR twice daily for 7 days
 - ↳ OR **Tab. Tinidazole 500mg** (Fasigyn, Trichogen, Prevent) 1-0-1 (BD), OR 2g x Once
 - Recommended Regimen:** Tinidazole 2g per oral by single dose OR twice daily for 7 days
- » **If women are pregnant (after first trimester for metronidazole) OR breast feeding**
 - ↳ **Cap. Clindamycin 300mg** per oral twice a day for 7 days
 - OR **Tab. Metronidazole 200mg** per oral TDS for 7 days
 - OR **metronidazole 0.75% vaginal applicator** (Metri-V) x intra-vaginally twice a day for 5 days

CANDIDA VAGINITIS (MONILIASIS)



- **Causative Organism:** Moniliasis is caused by *Candida albicans*, a gram-positive yeast-like fungus.
- **The risk factors for candida vaginitis are include:** Diabetes mellitus, pregnancy, Antibiotics (↓ Acid forming lactobacillus), Combined oral pills, Immunosuppression (HIV), steroids, Thyroid, parathyroid disease & Obesity

CLINICAL FEATURES

- The patient complains of vaginal discharge with intense vulvovaginal pruritus. The pruritus is out of proportion to the discharge. There may be dyspareunia due to local soreness.
- **On Examination**
 - The discharge is thick, curdy white and in flakes, (cottage cheese type) often adherent to the vaginal wall
 - Vulva may be red and swollen with evidences of pruritus.
 - Vaginal examination may be tender. Removal of the white flakes reveals multiple oozing spots.
 - Atrophy of the vulvovaginal structures are common in menopause due to deficiency of estrogen.

Diagnostic workup

- Wet smear of vaginal discharge is prepared. KOH solution (10%) is added to lyse the other cells (RBCs). Filamentous form of mycelia, pseudohyphae can be seen under the microscope.
- Culture in Nickerson's or Sabouraud's media – become positive in 24–72 hours.
- Women with recurrent vulvovaginitis, and vaginal boric acid capsule (600mg gelatin capsules) is effective
- Boric acid inhibits fungal cell wall growth.



TREATMENT OF CANDIDA VAGINITIS

- Corrections of the predisposing factors
- **Cap. Fluconazole 150mg** (Diflucan, Fungone) x Once orally single-dose only, or repeat day 7
- **Clotrimazole Vaginal cream/tablet** (Canesten, Gynosporin) x HS for 3-5 days
- **Use of Vegiwash** – Feminine intimate cleanser

BACTERIAL VAGINOSIS

- **Definition:** Bacterial vaginosis continues to be a leading cause of vaginitis (inflammation of the vagina). Clinically, it is characterized by milky vaginal discharge with fishy smell in the absence of any inflammation on biopsy of the vagina
- **Epidemiology:** most common vaginal infection in women (22–50% of all cases)
- **Pathogen:** The causative organism was previously thought to be *Gardnerella vaginalis* (*Haemophilus vaginalis*). The present concept is that along with *G. vaginalis*, anaerobic organisms such as *bacteroides* species, *peptococcus* species, *mobiluncus*, *prevotella* and *mycoplasma hominis* act synergistically to cause vaginal infection
- **Pathophysiology:** lower concentrations of *Lactobacillus acidophilus* lead to overgrowth of *Gardnerella vaginalis* and other anaerobes, without vaginal epithelial inflammation due to absent immune response.
- **Risk factors:** sexual intercourse (primary risk factor, but it is not considered an STD), intrauterine devices (IUD), vaginal douching, poor or excessive hygiene, OCPs, HIV infections, latex condom use, diabetes and pregnancy

Clinical features

- Commonly asymptomatic
- Increased vaginal discharge, usually gray or milky or creamy with fishy smell
- Dysuria, pruritus and pain are uncommon.

Diagnostic workup

Diagnosis is confirmed if three of the following

1. **Amsel criteria are met:**
 1. Vaginal pH: > 4.5
 2. **Wet mount microscopy of vaginal secretion:** Clue cells (Vaginal epithelial cells with a stippled appearance and fuzzy borders due to bacteria adhering to the cell surface).
 3. **Amine whiff test of vaginal secretion:** Positive
 - The addition of 1–2 drops of 10% potassium hydroxide to a sample of infected vaginal discharge emits a characteristic amine odor.
 4. Thin, homogeneous gray-white or yellow discharge that adheres to the vaginal walls



TREATMENT OF BACTERIAL VAGINOSIS

- **Asymptomatic:** reassurance; often resolves without treatment
- **Symptomatic patients**
 - **First-line in non-pregnant and pregnant patients:**
 - **Tab. Metronidazole 400mg** (Flagyl) x BD for 7 days OR intravaginal metronidazole 0.75% gel OR intravaginal clindamycin 2% cream x insert 5g (one applicatorful) into the vagina OD at night for 5 days
 - **Alternative in non-pregnant and pregnant patients:**
 - **Cap. Clindamycin 300mg** (Dalacin-C) x BD for 7 days
 - **Alternative in nonpregnant patients:** Tinidazole/Secnidazole
 - **Treatment of sexual partner(s) is not recommended.**

Complications

- **Adverse pregnancy outcomes:** Preterm delivery, spontaneous abortion, postpartum endometritis
- **Reinfection** (consider retesting after 3 months)



BARTHOLINITIS (INFECTIONS OF BARTHOLIN'S GLAND)

- Bartholin's glands are the two-pea sized (2 cm) glands, located in the groove between the hymen and the labia minora at 5 o'clock and 7 o'clock position of the vagina.
- Causative organisms:** Although Gonococcus is always in mind but more commonly other pyogenic organisms such as escherichia coli, staphylococcus, streptococcus, chlamydia trachomatis, bacteroides, peptostreptococcus or mixed types (polymicrobial) are involved.
- Pathology:** Both the gland and the duct are involved.
 - » The epithelium of the gland or the duct gets swollen.
 - » The lumen of the duct may be blocked or remains open through which exudates escape out.
- Fate:** The infection may resolute completely or an abscess is formed. In others, the infection subsides only to recur in future. In such cases, the gland becomes fibrotic. Too often, the duct lumen heals by fibrosis with closure of the orifice → pent up secretion of the gland → formation of Bartholin cyst. Thus, the end results of acute bartholinitis are: (a) Complete resolution; (b) Recurrence; (c) Abscess; (d) Cyst formation.

Clinical features & Diagnosis

- » Primarily a clinical diagnosis
- » Initially, there is local pain and discomfort even to the extent of difficulty in walking or sitting.
- » Examination reveals tenderness and induration of the posterior half of the labia when palpated between thumb outside and the index finger inside the vagina. The duct opening looks congested and secretion comes out through the opening when the gland is pressed by fingers.
- » The secretion should be collected with a swab for bacteriological examination.



TREATMENT OF BARTHOLINITIS

- Hot compress over the area
- Analgesics to relieve pain:**
 - ↳ Tab. Diclofenac sodium 50mg (Voren, Voltal) x BD/TDS
 - OR Tab. Naproxen sodium 500mg (Flexin, Neoprox) x BD
- Systemic antibiotic:** Appropriate antibiotic according to the bacteriological sensitivity should be instituted.
 - ↳ Tab. Amoxicillin/clavulanate 625mg (Augmentin, Calamox) x TDS
 - OR Cap. Cephalexin 500mg (Ceporex, Keflex) x BD
 - OR Cap. Cefixime 400mg (Cefim, Cefspan) x OD

- Recurrent bartholinitis:** Periodic painful attacks cause problems in 5–10% women. Excision of the gland with the duct may have to be done in the quiescent phase.

BARTHOLIN'S ABSCESS

Introduction: Bartholin's abscess is the end result of acute bartholinitis. The duct gets blocked by fibrosis and the exudates pent up inside to produce abscess. If left uncared for, the abscess may burst through the lower vaginal wall. A sinus tract may remain open with periodic discharge through it.

Clinical features & Diagnosis

- » Primarily a clinical diagnosis
- » Local pain & discomfort become intense.
- » The patient cannot walk or even sit.
- » Fever is often associated.
- » On examination, there is a unilateral tender swelling beneath the posterior half of the labia majora expanding medially to the posterior part of the labium minus. The overlying skin appears red and edematous.



TREATMENT OF BARTHOLIN'S ABSCESS

- Bed rest is imposed
- Analgesics to relieve pain:**
 - ↳ Tab. Diclofenac sodium 50mg (Voren, Voltal) x BD/TDS
- Systemic antibiotic:** Appropriate antibiotic according to the bacteriological sensitivity should be instituted.
 - ↳ Tab. Amoxicillin/clavulanate 625mg (Augmentin, Calamox) x TDS
 - OR Cap. Cephalexin 500mg (Ceporex, Keflex) x BD
 - OR Cap. Cefixime 400mg (Cefim, Cefspan) x OD
- Abscess should be drained at the earliest opportunity before it bursts spontaneously. In case of recurrent Bartholin's abscess, excision should be done in the quiescent phase after the infection is controlled

PELVIC ABSCESS



Definition: a pelvic abscess is an inflammatory collection of purulent material that forms secondary to an infection within the pelvis. Encysted pus in the pouch of Douglas is called pelvic abscess.

ETIOLOGY

PELVIC CAUSES (COMMON)

- » Postabortal and puerperal sepsis
- » Acute salpingitis
- » Perforation of an infected uterus such as attempted uterine curettage in septic abortion or pyometra
- » Infection of pelvic hematocoele usually following disturbed tubal pregnancy
- » Postoperative pelvic peritonitis following abdominal or vaginal hysterectomy
- » Irritant peritonitis following contamination of urine, bile, vernix caseosa, meconium (spilled during cesarean section), iodine containing dye used in hysterosalpingography or contents of ruptured ovarian cyst (sebum in dermoid cyst), etc.

EXTRA-PELVIC CAUSES (RARE):

- » Appendicitis, diverticulitis, ruptured gallbladder, perforated PUD, usually produce generalized peritonitis.
- » The condition may ultimately settle to the dependent pouch of Douglas and produces pelvic abscess.

CLINICAL FEATURES

» Patient can be ill from any of the causative factors mentioned earlier.

» But the localization of pus in the pouch of Douglas is evidenced by:

Symptoms

- » Spiky rise of high temperature with chills and rigor
- » Rectal tenesmus—frequent passage of loose mucoid stool
- » Pain lower abdomen—variable degrees
- » Urinary symptoms—difficulty or even retention of urine.

Signs

- » **General:** Pulse rate is raised out of proportion to temperature.
- » **Per abdomen**
 - Tenderness and rigidity in lower abdomen
 - A mass may be felt in the suprapubic region—tender, irregular, soft, and resonant on percussion.
- » **Per vaginam**
 - The vagina is hot and tender
 - The uterus is pushed anteriorly; the movement of the cervix is painful
 - A boggy, fluctuant, and tender mass is felt in the pouch of Douglas
 - A separate mass may be felt through the lateral fornix.
 - Rectal examination defines precisely the mass in the pouch of Douglas.

Diagnostic workup

- » **CBC:** High leukocytosis with ↑ polymorphs.
- » **Inflammatory marker:** Elevated ESR, Elevated CRP
- » **Culture and sensitivity (C&S):** Swabs are taken from high vagina, endocervical canal and from the pus
- » **Confirmation of diagnosis:** The diagnosis is easy in most of the cases but at times confusion arises between pelvic hematocoele and pelvic abscess.
- » **Pelvic ultrasound:** Reveals accumulation of fluid in the pouch of Douglas. Large amounts (normal is 10mL) of anechoic free fluid suggests inflammatory etiology.
- » **CT scan pelvis:** investigation of choice

Rx

» IV antibiotics for 24-48 hours than switch to oral (same as Bartholin's abscess): Antibiotic regimen may have to be changed depending upon the C&S report.

» Inj. Piperacillin-tazobactam 4.5g (Tanzo) x TDS

» Inj. Ceftriaxone 1g x (Oxidil, Titan) IV x BD
+ Inj. Metronidazole 500mg (Flagyl) x IV x TDS

» Analgesia

» Inj. Ketorolac 30mg/1ml (Toradol) x IV x TDS
OR Tab. Naproxen 500mg x orally, twice daily (BD)

» **Surgery:** Posterior colpotomy is the definitive surgery to drain the pus through posterior fornix. The loculi should be broken with finger. Laparotomy is done when the patient's condition deteriorates despite aggressive management. In patients with recurrent infection and with loss of reproductive function total abdominal hysterectomy with bilateral salpingo-oophorectomy is the preferred treatment. The pus should be sent for culture and drug sensitivity test



ATROPHIC VAGINITIS (SENILE VAGINITIS)

Genitourinary Syndrome of Menopause (GSM)

- Vaginitis in postmenopausal women is called atrophic vaginitis. The term is preferable to senile vaginitis. The vaginal defense is lost. Vaginal mucosa is thin due to deficiency of estrogen & is more susceptible to infection and trauma. There may be desquamation of the vaginal epithelium which may lead to formation of adhesions & bands between the walls.

ETIOLOGY

- Low estrogen levels: after menopause, B/L oophorectomy, radiotherapy, chemotherapy, immunological disorders
- Atrophy of epithelium in vagina and vulva

△ Atrophic vaginitis

C/C:

- Decreasing labial fat pad
- Discomfort, dryness, soreness in the vagina
- Dyspareunia, burning sensation after sex
- Yellowish discharge, occasional bleed spotting
- Commonly associated with receding pubic hair

Diagnostics: primarily a clinical diagnosis, additional tests (e.g., pH test, wet mount) are often nonspecific

Rx

TREATMENT OF ATROPHIC VAGINITIS

- If mild symptoms: Non-hormonal vaginal moisturizers and lubricants gel → Himalaya EveGel OR Vagisil Or Sesderma Or Membrasin Intimate Moisture Cream
- If moderate to severe symptoms: Vaginal estrogen therapy
 - Conjugated Estrogen Vaginal Cream (Premarin, Estromarin)
- Systemic hormone therapy if vasomotor symptoms
 - Tab. Conjugated Estrogen 0.3mg (Premarin)
 - Tab. Tibolone 2.5mg (Tibol, Livial, Lobion HRT)

PRIMARY DYSMENORRHEA (MENSTRUAL PAIN)

Definition: Dysmenorrhea is one of the most common gynecological symptoms affecting the quality of life of menstruating women. It is experienced as lower abdominal pain or uterine cramps that occur during the few days prior to and/or during menstruation, and usually subsides at the end of menstruation.

- Primary dysmenorrhea:** occurs in the absence of pelvic pathology. Prostaglandin-F (PGF) is the main contributor to the cause of dysmenorrhea. The time of the endometrial shedding during the beginning of menstruation is when the endometrial cells release PGF. Prostaglandin (PG) causes uterine contractions, and the intensity of the cramps is proportionate to the amount of PGs released after the sloughing process that started due to dropping hormonal surge.
- Secondary dysmenorrhea:** occurs in the presence of pelvic pathology due to an underlying disease, disorder, or structural abnormality either within or outside the uterus. There are many common causes of secondary dysmenorrhea – see below

CLINICAL FEATURES

- Recurrent, crampy, suprapubic pain occurring just before or during menses and lasting 2-3 days
- Spasmodic, crampy pain in the lower abdominal &/or pelvic midline may radiate into the lower back and thighs
- Headaches, diarrhea, fatigue, nausea, bloating & flushing are common accompanying symptoms
- Normal pelvic examination findings

Rx

TREATMENT OF PRIMARY DYSMENORRHEA

- Expectant management:** Assurance, Weight reduction, Encourage activities, regular exercise, To keep bowels empty, Maintaining an active lifestyle and a balanced diet – That is rich in vitamins and minerals, boiled eggs, hot milk, turmeric powder in hot milk → useful to reduce the intensity of the dysmenorrhea.
- NSAIDs:** Tab. Mefenamic Acid 500 mg (Ponstan Fort) x TDS OR Tab. Naproxen sodium 500mg (Neoprox, Flexin) x 500mg twice daily on day 1-3, then 250mg x twice daily.
- Suitable cases for medical therapy are:** Comparatively young age and having contraindications to 'pill'. The contraindications of medical therapy include allergy to aspirin, gastric ulceration and history of asthma.
- Oral contraceptive pills (OCPs) for 3-6 cycles:** Tab. Yaz x Once daily on day 3rd to 7th on menstrual cycle

The suitable candidates are patients	a) wanting contraceptive precaution	b) With heavy periods
	c) Unresponsive or contraindications to antiprostaglandin drugs.	
- Tab. Dydrogesterone 10mg (Duphaston)** x twice daily, it does not inhibit ovulation but probably interferes with ovarian steroidogenesis. It should be taken from day 5 of a cycle for 20 days. It should be continued for 3-6 cycles.
- The levonorgestrel-releasing intrauterine system (LNG-IUS):** LNG-IUS is very effective (50%) in reducing pain. It is used in women who desires contraception and where estrogen is contraindicated.
- If the above protocol fails, laparoscopy** is indicated to find out any pelvic pathology to account for pain (Endometriosis)
- DOC is NSAIDs** work best if taken at the first sign of your period or pain. You usually take them for only 1 or 2 days. Women with bleeding disorders, asthma, aspirin allergy, liver damage, stomach disorders, or ulcers should not take NSAIDs.
- Oral contraceptives** may be effective for relieving symptoms of primary dysmenorrhea, but evidence is limited.



SECONDARY DYSMENORRHEA

Definition: Secondary dysmenorrhea is normally considered to be menstruation—associated pain (recurrent lower abdominal pain shortly before or during menstruation) occurring in the presence of pelvic pathology.

Epidemiology

- » May begin later in life than primary dysmenorrhea
- » Commonly affects female individual's ≥ 25 years of age.

COMMON OF SECONDARY DYSMENORRHEA

Uterine causes	Extra-uterine causes
» Pelvic inflammatory disease (PID) » Intrauterine device (IUD) in utero » Adenomyosis » Uterine fibroids (intracavitary or intramural) » Cervical polyps, Cervical stenosis	» Endometriosis, Endometrial polyp » Pelvic adhesions, Pelvic congestion » Functional ovarian cysts » Inflammatory bowel disease (IBD) » Chronic pelvic infection

CLINICAL FEATURES

- » The pain is dull, situated in the back and in front without any radiation. It usually appears 3–5 days prior to the period and relieves with the onset of bleeding. There is no systemic discomfort unlike primary dysmenorrhea. The patients may have got some discomfort even in between periods.
- » Patient may present with few other gynecological symptoms like dyspareunia, dysuria, abnormal uterine bleeding and infertility.
- » Abdominal and vaginal examinations usually reveal the pathology.

DIAGNOSTIC APPROACH

- » **Diagnosis – Depend on the underlying cause**
- » **Detail history and Physical examination**
- » **Secondary dysmenorrhea should be suspected in the following cases:**
 - » Abnormal pelvic examination (E.g., uterine size, cervical motion tenderness, adnexal tenderness, masses, vaginal/cervical discharge)
 - » The pain tends to get worse over time.
 - » No previous history of pain with menstruation
 - » Infertility (Adhesions, Endometriosis, PID)
 - » Irregular cycles
 - » Heavy menstrual flow (e.g., adenomyosis, fibroids, polyps)
 - » Dyspareunia or postcoital bleeding
 - » Partial or no response to therapy with NSAIDs and/or hormonal contraceptives
- » **Investigations**
 - » **CBC with differential:** Anemia, infection
 - » **Urine D/R:** to rule out UTIs
 - » **Beta-hCG:** to rule out ectopic pregnancy.
 - » **Gonococcal/chlamydial swabs:** to rule out STDs and PID
 - » **Ultrasound Pelvic or Transvaginal US (TVUS)** – Can detect most pelvic pathology (Leiomyoma, adenomyosis).
 - » **Saline infusion sonography:** May reveal submucous fibroid, polyps.
 - » **Laparoscopy (endometriosis, PID):** Useful for both diagnostic and therapeutic purposes.
 - » **Hysteroscopy** is useful for both diagnostic and therapeutic purposes.

Rx

TREATMENT OF SECONDARY DYSMENORRHEA

- » The treatment aims at the cause rather than the symptom.
- » The type of treatment depends on the severity, age and parity of the patient.



PREMENSTRUAL SYNDROME (PMS)

- Definition: PMS is a psychoneuroendocrine disorder of unknown etiology, often noticed just prior to menstruation. Many women feel physical or mood changes during the days before menstruation. When these symptoms happen month after month, and they affect a woman's normal life, they are known as premenstrual syndrome (PMS). There is cyclic appearance of a large number of symptoms during the last 7–10 days of the menstrual cycle.
- Etiology: Several biological factors like estrogen, progesterone, neurotransmitters—gamma Aminobutyric acid (GABA), serotonin and the renin-angiotensin–aldosterone system (RAAS) are thought to be involved.

Diagnosis

- PMS is more common in women aged 30–45. It may be related to childbirth or a disturbing life event. There are no abnormal pelvic findings excepting features of pelvic congestion. Occurs in up to 12% of female individuals.
- Diagnosis is based on history and self-assessment (maintaining a PMS diary)
- Preexisting thyroid disorders and psychiatric (major depressive disorder) conditions should be ruled out.

	Premenstrual syndrome (PMS)	Premenstrual dysphoric disorder (PMDD)
Definition	» The onset of severe discomfort or functional impairment prior to menstruation	» Severe affective symptoms and behavioral changes that cause clinically significant disturbance of daily life
Diagnostic criteria	» Present in the 5 days prior to the beginning of menstruation for at least 3 consecutive cycles » End within 4 days after the beginning of menstruation » Interfere with normal daily life activities	» Present up to 7 days prior to the onset of menstruation for the majority of cycles within one year » ≥ 5 symptoms that are marked and/or persistent (e.g., depressed mood, anxiety, anger, affective lability, sleep disturbances, change in appetite, pain, headache) » Significant interference in daily life (work, home, social activities, interpersonal relationships)

△ Premenstrual syndrome (PMS) C/C:

- » Onset of symptoms 5 days before menstruation
- » **Pain:** dyspareunia, breast tenderness, headache, back pain, abdominal pain
- » **Gastrointestinal changes:** nausea, diarrhea, changes in appetite (food cravings)
- » Bloating and weight gain
- » Tendency to edema formation
- » **Neurological:** migraine, increased sensitivity to stimuli
- » **Psychiatric:** mood swings, drowsiness, lethargy, exhaustion, depression, anxiety, aggressiveness, social withdrawal

» **Treatment with Progesterone for PMS and post-natal depression:** → The recommended dose is 200 mg once a day or 400 mg twice a day by vaginal or rectal insertion. But according to DC Dutta's, it is not effective in treating PMS.

» **N.B.** When the symptoms are severe and/or the treatment fails, psychiatric referral should be done.



1. Lifestyle changes can be beneficial

- » Patient education and counselling
- » cognitive behavioral therapy – a talking therapy
- » Regular exercise, healthy diet and dietary supplements
- » Avoid triggers like alcohol, caffeine, nicotine and smoking
- » Get plenty of sleep 7 to 8 hours is recommended
- » Advise patients keep a diary/record of symptoms for at least 2 to 3 menstrual cycles – you can take this to a GP appointment

2. **Tab Mefenamic acid 500mg** (Mefnac DS, Ponstan Fort) x TDS
OR **Tab. Naproxen sodium 500mg** (Flexin, Synflex)
1 – 0 – 1, initially 500mg BD day 1-3, then 250mg x BD

» **Consider Oral contraceptive pills (OCPs) for 3–6 cycles**
Tab. Ethinyl Estradiol 0.02mg + Drospirenone 3mg (Tab. Yaz)
» Once daily on day 3rd to 7th on menstrual cycle

3. **Tab. Ossein mineral complex + Vitamin-D3** (Calone-D, Osante-D)
OR **Tab. Multivitamins** (Theragran ultra, Vitrum, Surbex-2)

Antidepressants (SSRIs) in the case of severe PMS and PMDD

4. **Cap. Fluoxetine 20mg** (Depex, Flux) x OD
OR **Tab. Sertraline 50mg** (Fredep, Sert) x OD
Once daily after breakfast, may consider gradually increasing dose after several weeks by 20mg/day. (Max dose is 60–80mg)
&/or **Tranquillizers: Tab. Alprazolam** at dose 0.25mg to 0.5mg x HS

MITTELSCHMERZ'S SYNDROME (OVULATORY OR MIDCYCLE PAIN)



- Definition:** Ovular pain is not an infrequent complaint. The pain is usually situated in the hypogastrium or in either of the iliac fossa. Physiological preovulatory pain in female individuals of reproductive age.
- Epidemiology:** occurs in approximately 40% of female individuals of reproductive age.
- Etiology:** The exact cause is not known. The probable factors are: (a) Increased tension of the Graafian follicle just prior to rupture; (b) Peritoneal irritation by the follicular fluid following ovulation; and (c) Contraction of the tubes & uterus.

△ Mittelschmerz's

- C/C:**
- Recurrent unilateral lower abdominal pain (can mimic appendicitis)
 - Pain occurs during midcycle in individuals with regular menses.
 - Dull & achy pain which can become cramp-like
 - It rarely lasts > 12 hours (Can last up to 3 days)
 - It may be associated with slight vaginal bleeding or excessive mucoid vaginal discharge
 - On abdominal palpation:** Lower abdominal pain

Rx

(Anafortan Plus, Spasfon, Spasrid)

1. Tab. Phloroglucinol + Trimethylphloroglucinol

Consider NSAIDs if severe or not respond

2. Tab Mefenamic acid 500mg (Ponstan Forte) x TDS
OR Tab. Naproxen sodium 500mg (Flexin, Neoprox) x BD
Initially 500mg twice daily on day 1-3, then 250mg x BD

In obstinate cases, the cure is absolute by making the cycle anovular with contraceptive pills.

MENORRHAGIA

Rx

Treat underlying cause (see etiology of secondary dysmenorrhea)

1. Tab Mefenamic acid 500 mg (Mefnac DS, Ponstan Fort) x TDS
OR Tab. Naproxen sodium 500mg (Flexin, Synflex) x Initially 500mg BD day 1-3, then 250mg x BD
2. Consider to stop acute bleeding: Cap. Tranexamic acid 500mg (Transamine, Traxacid) x BD/TDS
3. Other medications
 - » COCP (Tab. Yaz, Tab. Diane-35, Tab. Progyluton) x Once daily for 21 days than 7 days break x 3 months
 - » OR Tab. Norethisterone 5mg (Tab. Primolut-N, Tab. Noregyn) x Three time daily

GUIDELINES – NORETHISTERONE: 1 tablet x TDS (15 mg) for 10 days. After stop taking the tablets, patient will usually have bleeding like a period. To stop periods causing problems again, Doctor may tell the patient to take Norethisterone tablets for a few days after your next two periods. Advice to take 1 tablet 5mg x twice a day (10 mg) for 8 days. Patient will need to start taking these tablets 19 days after her last period began.

OLIGOMENORRHEA

- Definition:** Influent menstrual periods
- Causes:** PCOS, Cushing syndrome, Prolactinoma, PID, Asherman syndrome, hyperthyroidism, CAH.

△ Oligomenorrhea

- C/C:**
- Menstrual period at interval of > 35 days.
 - Usually light menstrual flow
 - Irregular menstrual periods with unpredictable flow
 - Fewer more than 6 to 8 periods over year

Diagnostic workup: CBC, HBA1C, TSH, LH, FSH, serum prolactin, testosterone level and USG pelvis

Rx

Treat underlying cause

First line drug if no underlying pathology

- » Tab. Dydrogesterone 10mg (Duphaston)
I – 0 – I (BD)



ENDOMETRIOSIS

Definition: Endometriosis is a chronic inflammatory condition defined by presence of functioning endometrium (glands and stroma) found outside of the uterine cavity. The most common sites affected are the pelvic peritoneum & ovaries. It is not a neoplastic condition, although malignant transformation is possible.

ETIOLOGY

- » The etiology of endometriosis is not yet fully understood; however, retrograde menstruation seems to play a major role in the pathogenesis of endometriosis.
- » **Other contributing factors include:** Coelomic metaplasia, iatrogenic implantation, Hematogenic & lymphogenic dissemination of endometrial cells, hereditary component.
- » **Risk factors:** Nulliparity, Prolonged exposure to endogenous estrogen (early menarche, late menopause), Short menstrual cycles (< 27 days), Menorrhagia (> 1 week), Family history

CLINICAL FEATURES

Clinical presentation: Typical symptoms + Involvement of GIT + Bladder symptoms

Typical symptoms

- » Dysmenorrhea (70%)
- » Abnormal uterine bleeding (AUB) (15-20%)
- » Chronic or cyclical pelvic pain that worse before and after periods (menses).
- » **Deep dyspareunia:** Deep pain during or after sexual intercourse
- » Subfertility (40-60%)

Period-related or cyclical gastrointestinal symptoms

- » Abdominal pain
- » GIT Upsets
- » Tenesmus
- » Painful defecation (dyschezia)
- » Diarrhea/Constipation
- » Rectal bleed/melena

Period-related or cyclical urinary symptoms

- » Frequency
- » Dysuria (Pain passing urine)
- » Obstruction
- » Hydronephrosis
- » Back pain
- » Haematuria (Blood in urine)

DIAGNOSTIC APPROACH

Clinical diagnosis: It is made often by the classic triad of symptoms of progressively increasing secondary dysmenorrhea, dyspareunia, and infertility/subfertility. This is corroborated by the pelvic findings. Age of onset 20-40 years.

- » **Abdominal examination:** Abdominal palpation may not reveal any abnormality. A mass may be felt in the lower abdomen arising from the pelvis—enlarged chocolate cyst or tubo-ovarian mass due to endometriotic adhesions. The mass is tender with restricted mobility.
 - » **Pelvic examination:** Bimanual examination may not reveal any pathology. The expected positive findings are—pelvic tenderness, nodules in the pouch of Douglas, nodular feel of the uterosacral ligaments, fixed retroverted uterus or unilateral or bilateral adnexal mass (chocolate cyst) of varying sizes.
 - » **Speculum examination:** may reveal bluish spots in the posterior fornix.
 - » **Rectal or rectovaginal examination** is often helpful to confirm the findings.
 - » **Serum CA-125 level:** a moderate elevation of serum CA 125 is noticed in patients with severe endometriosis. It is not specific for endometriosis, as it is significantly raised in epithelial ovarian carcinoma. However, it is helpful to assess the therapeutic response and in follow-up of cases and to detect any recurrence after therapy.
 - » **Monocyte Chemotactic Protein (MCP-1) level** is increased in the peritoneal fluid of women with endometriosis.
 - » **Best initial test is Transvaginal ultrasound (TVUS):** The uterus is generally not enlarged, Evidence of ovarian cysts (chocolate cysts), Nodules in bladder or rectovaginal septum.
 - » **Best diagnostic test is MRI Pelvis:** Sensitivity and specificity of MRI is 91-95%. It is superior compared to TVUS and CT scan with much better resolution and soft tissue interfaces. MRI is better to diagnose deeply infiltrative endometriosis (DIE), and deep seated endometrioma. MRI can detect extra-pelvic and rectovaginal implants.
- Findings:** hypointense, irregular thickening or mass of uterosacral ligament; replacement of fat tissue plane between uterus and rectum/sigmoid with tissue mass.
- » **Diagnostic test: Laparoscopy (Gold standard test):** direct visualization with biopsy-confirmed endometrial glands or stroma outside of the uterine cavity.
 - » **Early stage (minimal to mild):** Marked by superficial peritoneal implants which appear vesicle-like (clear or red).
 - » **Moderate disease:** Characterized by multiple superficial or deep lesions with a variable degree of adhesions
 - » **Advanced disease:** Typified by multiple implants (deep and fibrotic), parametrial or retroperitoneal extension, ovarian endometrioma, an obliterated cul-de-sac and pelvic adhesions.

DIFFERENTIAL DIAGNOSIS

- | | |
|--|------------------------------|
| » Adenomyosis | » Ovarian cyst (benign) |
| » Pelvic inflammatory disease (PID) | » Ovarian cancer, epithelial |
| » Interstitial cystitis & irritable bowel syndrome | » Uterine myoma (fibroids) |

TREATMENT OF ENDOMETRIOSIS

Endometriosis needs to be treated as it is a progressive disease (30–60%).

Preventive

The following guidelines may be prescribed to prevent or minimize endometriosis:

- » To avoid tubal patency test immediately after curettage or around the time of menstruation.
- » Forcible pelvic examination should not be done during or shortly after menstruation.
- » Married women with family history of endometriosis are encouraged not to delay the first conception but to complete the family.

Curative

The objectives are:

- » To abolish or minimize the symptoms—pelvic pain and dyspareunia
- » To improve the fertility
- » To prevent recurrence and disease progression
- » To improve the quality of life

TREATMENT OPTIONS FOR PELVIC ENDOMETRIOSIS

» **Expectant management:** Endometriosis is a progressive disease in about 30–60% of women. It is not possible to predict in which woman it will progress. Some form of treatment is often needed to arrest the progress of the disease. However, in women with minimal to mild endometriosis role of any treatment is controversial. Cumulative pregnancy rate is similar when expectant treatment is compared with conservative surgery.

» **Case selection is important for expectant treatment**

- » Minimal endometriosis with no other abnormal pelvic finding
- » Unmarried
- » Young married who are ready to start family
- » Approaching menopause

» **Protocols for Expectant Management**

- » Observation with administration of nonsteroidal antiinflammatory drugs (NSAIDs) or prostaglandin synthetase inhibiting (PSI) drugs are used to relieve pain.
 - » Tab. Naproxen 250–500 mg (Flexin) orally twice daily or Tab. Ibuprofen 400mg (Brufen) three time daily or Tab. Mefenamic acid 250–500mg (Ponstan) three time a day is quite effective.
- » The married women are encouraged to have conception. Pregnancy usually improves the condition due to absence of shedding & decidual changes in the ectopic endometrium causing its necrosis & absorption.

Immediate fertility not desired: pain without endometrioma or suspected severe/deep disease

1. First-line treatment

- » **Combine oral contraceptive pills (COCP):** Duration 6 – 12 months (Shut down hypo-pituitary ovarian axis)
 - » Tab. Ethinyl estradiol 0.03mg + Levonorgestrel 0.15mg + Ferrous Fumarate 75mg (Famila-28F, Novodol) OR Tab. Ethinyl Estradiol 0.02mg + Drospirenone 3mg (Tab. Yaz) x Start from 1st day of periods and continue it according to instruction over the pack.
 - » **OR Progestogens: ONE of the following Progestogens**
 - » Inj. Medroxyprogesterone acetate 150mg (Depo-Provera) x IM every 3 months for 6–9 months
 - » Tab. Medroxyprogesterone acetate 10mg (Provera) x Three time daily, orally for 6–9 months
 - » Tab. Dydrogesterone 10mg (Duphaston, D-Gest, Dirogest) x Twice daily for 6–9 months
 - » Tab. Norethisterone 5mg (Primolut-N, Noregyn) at dose 10–20mg orally BD/TDS for 6–9 months
- » **± Adjunctive NSAIDs:** Tab. Naproxen 500mg (Flexin, Neoprox) x Twice daily, orally

2. Second-line treatment

- » **Androgenic agonists:** Cap. Danazol 200 mg (Danzol, Danocrine) at dose 400 – 600 mg per orally in 4 divided doses for 6 – 9 months (less tolerated)
 - » OR Cap. Gestrinone 2.5mg (Dimetriose) at dose 1.25 or 2.5 mg twice a week 6–9 months (well tolerated)
 - » Same mechanism of action (MOA) like that of Danazol and less side effects than Danazol.
- » **OR Gonadotropin-releasing hormone (GnRH) agonist analogue:** For 6 months duration, repeat course shouldn't be given due to concern about loss of bone mineral density
 - » Inj. Leuprolide acetate 3.75 mg (Lutrate Depot 3.75) x IM x used every month for 3 months



- » OR Inj. Leuprolide acetate 22.5 mg (Lutrate Depot 22.5) x used once in three month.
- » OR Inj. Goserelin acetate 3.6mg (Zoladex 3.6mg) x SC (into the anterior abdominal wall), once every 28 days for up to 3 months OR Inj. Goserelin acetate 10.8mg (Zoladex 10.8mg) x SC (into the anterior abdominal wall) once every 12 weeks. These drugs are not recommended for more than 6 months
- » **Adjunctive NSAIDs:** Tab. Naproxen 250 – 500 mg (Flexin) per orally twice daily
- » **Adjunctive Laparoscopy**

3. Third-line treatment

» **Hysterectomy**

- » Ovarian endometriomas do not resolve in response to hormonal suppression and, if symptomatic, should be addressed surgically. Radical excision of affected areas with restoration of normal anatomy is the preferred method of treating symptomatic women with deep peritoneal disease.
- » Improvement in pain may last up to 5 years after surgery, but the risk of reintervention approaches 50% in women with moderate to severe disease.
- » Less aggressive surgical measures and younger age are predictive of recurrence.
- » For this reason, prolonged hormonal suppression is recommended after surgery for endometriosis.

» **Hormonal therapy**



IMMEDIATE FERTILITY DESIRED PATIENTS

» **First-line treatment → Controlled ovarian hyperstimulation**

- » **Tab. Clomiphene citrate 50mg** (Clomid, Ovafrin, Ovi-F) at dose 50-200mg per orally (PO) once daily for 5 days OR **Tab. Letrozole 2.5mg** (Femara, Lets, Retzole) at dose 5-7.5mg, starting on day 3 of cycle, once daily for 5 days
- » **Alternative option (Secondary)**
 - » Inj. Menotropins 75-225 international units subcutaneously/intramuscularly once daily
 - » OR Inj. Follitropin alfa 75-225 international units subcutaneously once daily
- » **Adjunctive therapy: NSAIDs → Tab. Naproxen 500 mg** (Flexin, Neoprox) x orally twice daily
- » **Adjunctive: Therapeutic Laparoscopy** (Laparoscopy significantly improves natural conception rates.)

» **Second-line treatment**

- » **In vitro fertilization (IVF)**
- » **Adjunctive therapy: NSAIDs → Tab. Naproxen 250 – 500 mg** (Flexin) per orally twice daily
- » **Adjunctive: Therapeutic Laparoscopy**



SURGICAL MANAGEMENT OF ENDOMETRIOSIS

Surgery may be conservative or definitive.

» **Indications of surgery**

- » Endometriosis with severe symptoms unresponsive to hormone therapy.
- » Severe and deeply infiltrating endometriosis (DIE) to correct the distortion of pelvic anatomy.
- » Severe endometriosis with pelvic adhesive disease.
- » Endometriomas of more than 1 cm.

» **First-line: Laparoscopic excision and ablation of endometrial implants.**

- » Reproductive (fertile) female
- » To confirm the diagnosis and exclude malignancy
- » To treat patients who do not respond to pharmacological therapy
- » **Treat expanding endometriomas & complications:** bowel/bladder obstruction, rupture of endometrioma, infertility

» **Second-line: Open surgery with hysterectomy with or without bilateral salpingo-oophorectomy**

- » Treatment-resistant symptoms
- » No desire to bear additional children (completed family)

» **Combined medical and surgical treatment**

- » **Preoperative hormonal therapy:** aims at reduction of the size and vascularity of the lesion which facilitate surgery.
- » The idea of postoperative hormonal therapy is to destroy the residual lesions left behind after surgery and to control the pain. But it does not improve fertility. It is generally avoided.

» **Duration of therapy** is usually 3-6 months preoperatively and 3-6 months postoperatively.

UTERINE FIBROIDS (UTERINE LEIOMYOMAS)

Definition: Uterine fibroids are benign tumors of the uterus primarily composed of smooth muscle and fibrous connective tissue. Grossly, these tumors are round, firm, and well-circumscribed nodules located just under the uterine serosa (subserosal), within the myometrium (intramural) or just below the endometrium (submucosal).

Risk factors: Obesity, Age in the 40s, black women, nulliparity, vitamin D deficiency, poor vitamin-A intake, smoking

Clinical features

Most women have small, asymptomatic fibroids.

Symptomatic <50%, Symptoms depend on the number, size, and location of leiomyomas.

Abnormal menstruation: Hypermenorrhea, heavy menstruation; metrorrhagia (associated anemia), dysmenorrhea

Features of mass effect:

• Pelvic mass along with dragging sensation due to back or pelvic pain/pelvic pressure symptoms/discomfort

• **Urinary tract symptoms:** urinary frequency, urinary retention, features of hydronephrosis.

• **Bowel symptoms:** bloating, constipation, haemorrhoids

• Infertility (difficulty conceiving and increased risk of miscarriage), dyspareunia, post coital bleed.

• Features of Iron deficiency anemia secondary to chronic blood loss.

On physical examination: Pallor, varicose vein, pedal edema, enlarged, firm and irregular uterus, ↑ fundal height, during bimanual pelvic examination

Diagnostic workup

First-line test: Ultrasound transvaginal and transabdominal views of the pelvis to ensure uterine pathology → May shows concentric, hypoechoic, heterogeneous tumors calcifications or cystic areas suggest necrosis.

Additional test: CBC, urea, creatinine, urine D/R.

Saline-infused sonography (Sonohysterography): Better visualize submucosal and intramural fibroids

Hysteroscopy: space-occupying lesions of the endometrial cavity such as endometrial polyps and submucosal fibroids

MRI: to evaluate the uterus and ovaries for potentially complicated surgical cases and visually differentiate between leiomyomas, adenomyomas, and adenomyosis.



TREATMENT OF UTERINE LEIOMYOMAS (UTERINE FIBROIDS)

• If asymptomatic fibroid: Observation, follow up, Fibroids can shrink substantially postpartum and after menopause.

• If symptomatic fibroid → Medical treatment

• Drug which decreases blood loss by decreasing the size of fibroid by which either ↓ estrogen production (GnRH agonist) or ↓ progesterone production (anti-Progesterone or SPRM) to shrink fibroids before surgery.

• **GnRH agonist:** Inj. Leuprolide (Lucrin Depot, Lorelin Depot, Lectrum) at dose 3.75mg, IM once monthly for up to 3 months OR 11.25mg, IM as a single dose OR Inj. Goserelin acetate 3.6mg (Zoladex 3.6mg) x SC (into the anterior abdominal wall), once every 28 days for up to 3 months OR Inj. Goserelin acetate 10.8mg (Zoladex 10.8mg) x SC (into the anterior abdominal wall) once every 12 weeks. These drugs are not recommended for more than 6 months

• **OR Anti-Progesterone:** Tab. Mifepristone at dose 2.5mg to 10mg orally for 3 – 6 months.

• **OR Selective progesterone receptor modulator (SPRM):** Tab. Ulipristal acetate 5mg (Fibristal) x at dose 5 mg to 10 mg x orally once daily, the efficacy of this same as GnRH agonist.

• **For correction of Anemia:** Iron supplementation → Tab. Iberet Folic OR Cap. Fefolvit x once daily

• **For dysmenorrhea:** Tab. Naproxen sodium 500mg (Flexin, Neoprox) x twice daily, when needed.

• **Drug which decreases Blood loss but do not have any effect on size of fibroid**

• **Cap. Tranexamic acid 500mg (Transamine) x three time daily for 5 days during monthly menstruation**

• **OR Ethinyl Estradiol 0.02mg + Drospirenone 3mg (Tab. Yaz) x Start once daily from 1st day of periods.**

• **OR Levonorgestrel intrauterine device (Mirena IUS-52) insert 52mg device into uterine cavity, remove and replace (if necessary) after 6 years.**

• **Surgical management**

• **Myomectomy** – to preserves fertility with adjunct pre-operative medical treatment as explain above

• **Treatment options for those where fertility is no longer required, adjunct pre-operative medical treatment**

• **Interventional therapy** → Uterine artery embolization: a percutaneous, radiologic procedure in which an embolic agent is injected into the uterine artery in order to block the blood supply to the fibroids

• **Definitive treatment:** Hysterectomy with/without bilateral salpingo-oophorectomy



FEMALE INFERTILITY

ETIOLOGY

Ovary-related causes

- » Premature ovarian failure
- » Menstrual cycle abnormalities (Functional hypothalamic amenorrhea)
- » Hyperprolactinemia
- » Thyroid disorders
- » **Systematic Conditions:** Diabetes mellitus, hypertension, obesity, chronic hepatic or renal disease
- » Pituitary adenoma
- » **Diminished Ovarian Reserve:** A decline in functioning oocytes (either reduced number or impaired development), a normal consequence of age, but can also be caused by an underlying disorder (Endometriosis)
- » Hypogonadotropic hypogonadism
- » Cushing syndrome
- » Polycystic Ovary Syndrome (PCOS)

Tubal/Pelvic causes

- » Pelvic inflammatory disease (PID)
- » Endometriosis
- » Fallopian tube adhesions and/or obstruction
- » Following tubal or pelvic surgery
- » **Following Infections:** appendicitis, chronic chlamydia infection, acute salpingitis, inflammatory bowel disease.

Uterine causes

- » Anatomical anomalies (septate uterus, bicornuate uterus, Mayer-Rokitansky-Kuster-Hauser syndrome)
- » Uterine leiomyoma
- » Endometrial polyps
- » **Asherman Syndrome:** Mostly iatrogenic (scarring, fibrosis, and/or adhesions of the endometrium caused by curettage). Reduces the sensitivity of the endometrium to progestogens

Cervical causes

- » Cervical anomalies (e.g., insufficient cervical mucus production)
- » Trauma (following cryotherapy, conization)
- » Immune factors (antisperm antibodies in the cervical mucus)
- » DES exposure in utero

Psychiatric causes:

- » Vaginismus
- » Sexual arousal disorder

DIAGNOSTIC APPROACH

- » Medical history of both partners, especially gynecological history (Children, family history), Tuberculosis, sexually transmitted infections, Hypothyroidism, features suggestive of pelvic inflammation or diabetes.
- » The surgical history should be directed especially towards abdominal or pelvic surgery
- » **Assessment of ovulatory function**
 - » **Menstrual history:** Should be taken in details. Wide spectrum of abnormalities ranging from hypomenorrhea, oligomenorrhea to amenorrhea are associated with disturbed hypothalamo-pituitary ovarian axis. This may be either primary or secondary to adrenal or thyroid dysfunction.
 - » Body temperature analysis to monitor menstrual cycle
 - » **Hormone tests (between the 3rd and 5th day of the menstrual cycle)**
 - » **Mid-luteal serum progesterone levels:** Progesterone should increase shortly after ovulation ($> 3 \text{ ng/mL}$ = recent ovulation) $\rightarrow$ Failure of progesterone levels to rise ($< 3 \text{ ng/mL}$) indicates anovulation, so evaluate for causes of anovulation i.e. PCOS, hyperprolactinemia, hypothyroidism
 - » **Ovulation prediction test** (detect LH levels)
 - » **Androgen levels:** Elevated levels induce negative feedback to the hypothalamus $\rightarrow$ inhibition GnRH secretion $\rightarrow$ decreased estrogen levels and suppression of ovulation
 - » **Ovarian reserve**
 - » **Early follicular FSH levels:** Elevated in ovarian insufficiency and indicate reduced ovarian reserve
 - » **Early follicular estradiol levels**
 - » **Anti-Müllerian hormone levels**
 - » **TSH levels:** $\uparrow$ levels in hypothyroidism
 - » **Prolactin levels:** Raised level = Hyperprolactinemia
 - » **Ovarian sonography:** Antral follicle count



- » **Endometrial biopsy**
 - Usually performed 1–3 days before menstruation to determine thickness of endometrium
 - A flat endometrial lining indicates a defect in the luteal phase of the menstrual cycle.
- » **Radiological investigations:** assess the patency of fallopian tubes and uterus
 - » **Indications**
 - If the initial workup does not reveal any abnormalities and no history suggestive of tubal obstruction
 - Screen for tubal occlusion and structural uterine abnormalities (septate uterus, submucous fibroids, intrauterine adhesions)
 - » **Hysterosalpingography:** an imaging technique involving the injection of contrast dye into the cervical canal and serial radiographs to evaluate the uterine cavity and Morphology/Patency of the fallopian tubes
 - » **Sonohysterosalpingography:** an ultrasound technique in which fluid is inserted into the uterus via the cervix to examine the uterine lining
 - » **Hysteroscopy and/or laparoscopy:** Indicated if there is evidence of intrauterine abnormalities or tubal occlusion. Can also be used therapeutically to remove small adhesions or mucous plugs obstructing the tubal lumen
- » **Examination of cervix:** Physical examination, pap smear, testing for antisperm-antibodies in cervical mucus

△ Female Infertility

C/C:

Female infertility may manifest with symptoms of anovulation (e.g., amenorrhea, irregular menses).

ASSISTED REPRODUCTIVE TECHNOLOGY

In vitro fertilization

- » The most common form of assisted reproduction technology
- » Involves hormonal follicular stimulation followed by a transvaginal follicular puncture for oocyte retrieval with ultrasound monitoring
- » The recovered oocytes are mixed with processed spermatozoa and incubated.
- » Two (in young women) to a maximum of five embryos (in women over 40 years of age) are transferred into the uterus.

Intracytoplasmic sperm injection: a type of assisted reproductive technology, in which a single spermatozoon is introduced into an oocyte under a microscope using an injection pipette

Intrauterine insemination (IUI): a procedure in which washed and concentrated sperm are introduced directly into the uterine cavity

Oocyte donation

Surgery: removal of tubal, cervical, or uterine adhesions, myomas, and/or scar tissue



TREATMENT OF FEMALE INFERTILITY

- » **Lifestyle modifications:** cessation of alcohol, smoking, nicotine, and recreational drug use as they contribute to subfertility.
- » **Treatment of underlying causes**
 - » **For Hypothyroidism:** Tab. Levothyroxine 25mcg, 50mcg, 75mcg and 100mcg (Thyronorm) see endocrinology
 - » **For Hyperprolactinemia:** Tab. Bromocriptine 2.5mg (Brotin, Parlodel) or Cabergoline (Dostinex)
 - » **For PCOS:** Tab. Metformin 500mg OR 850mg (Glucophage) x BD
- » **Ovulation induction**
 1. **Tab. Clomiphene citrate 50mg** (Clomid, Ovafrin, Ovi-F) from the 2nd to 6th day of menstrual cycle, can be used up to 6 to 12 cycle. Dosage maybe increased to 200mg/day depending upon the response. Monitoring is done by transvaginal ultrasonography (TVUS). Ovulation rate = 70%.
 2. **Aromatase Inhibitors: Tab. Letrozole 2.5mg** (Femara, Lets, Retzole, Aromek) x 2.5mg to 5mg x OD from the 2nd to 6th day of cycle. **Ovulation should occur between days 14 to 19** (so please have intercourse beginning around day 12 and don't skip two days in a row through at least day 20). In the first cycle of Letrozole, you should have a blood progesterone level drawn 5 to 7 days after ovulation. If you get an excellent response from Letrozole (ovulation & excellent progesterone level) than we'll continue **Letrozole** for 3 to 4 cycles.
 3. **Injection of Gonadotropin-releasing hormone (GnRH) analogs and GnRH antagonists:** Stimulation of FSH and LH release → Follicle maturation.
 4. **Injection of Human menopausal gonadotropin (hMG) 75IU or 150IU** (Menopur, IVF-M, Ferti-M, Repronex, Pergonal): stimulate final oocyte maturation → Ovulation
 5. **Selective Estrogen Receptor Modulator (SERM):** Tab. Tamoxifen 10mg or 20mg (Nolvadex, Zymoplex)



POLYCYSTIC OVARY SYNDROME (PCOS)

Pathophysiology of polycystic ovary syndrome (PCOS)

- » The exact pathophysiology is unknown.
- » Strong association with **OBESITY** → ↓ number of insulin receptors (down regulation) → peripheral sensitivity to insulin (peripheral insulin resistance) → Elevated insulin level → hyperinsulinemia leads to increased insulin-like growth factor-1 (IGF-I) expression in fibroblast → increase fibrous tissue formation in:
 - ↳ **Skin** → **Acanthosis nigricans** (Hyperpigmentation of the skin and Velvety skin appearance)
 - ↳ **Ovaries** → Polycystic ovaries.

DIAGNOSTIC APPROACH

- » **Rotterdam criteria:** (According to the American Association of Clinical Endocrinologists)
PCOS is diagnosed in adults based on the presence of at least two of the following criteria, after other Endocrinological conditions, E.g., thyroid disease, hyperprolactinemia, have been excluded.
 1. Oligoovulation and/or anovulation
 2. **Hyperandrogenism:** based on clinical features or laboratory test (Elevated level of Testosterone, Androstenedione and Dehydroepiandrosterone sulfate) → Examine patients for signs of acne, alopecia, and hirsutism and obtain laboratory studies as needed.
 3. **Enlarged and/or polycystic ovaries on pelvic ultrasound:**
 - » Ovarian volume ≥ 10 mL
 - » And/or the presence of multiple cystic follicles measuring 2–9mm (string-of-pearls appearance) in one or both ovaries.
- » **Obtain blood hormone levels**
 - » Total and free Testosterone: ↑
 - » Serum LH & FSH level: ↑ LH (LH:FSH ratio $>2:1$)
 - » Estrogen level: normal or slightly elevated
- » **Rule out other causes:**
 - » Fasting blood sugar (FBS): Normal value 80–120mg/dl
 - » Hemoglobin A1C (HbA1C): Normal value ($<5.7\%$), Pre-Diabetes (5.7% – 6.4%), Diabetes ($>6.4\%$)
 - » Prolactin level: Normal or may be elevated
 - » Fasting lipid profile (FLP)
 - » Serum or Urine pregnancy test
- » **Ovarian ultrasonography**
 - » **Transvaginal:** (preferred; use if acceptable to patient): offers the best visualization of ovarian follicles
 - » **Transabdominal:** should focus on measuring ovarian volume

CLINICAL FEATURES

1. Onset of symptoms typically occurs during young age (adolescence).
2. **Menstrual irregularities:** Primary or secondary amenorrhea, Oligomenorrhea, Menorrhagia
3. **Skin manifestation:**
 - » **Hirsutism:** Excessive male pattern hair growth on women on chin, upper lip, chest, around umbilicus.
 - » **Androgenic alopecia:** hair loss caused by the effect of dihydrotestosterone on the hair follicle, resulting in a characteristic pattern of balding (bitemporal scalp in men and vertex and frontal scalp in women).
 - » Acne vulgaris (Acne on face, chest &/or back)
 - » **Acanthosis nigricans:** appearance of velvety hyperpigmentation in the axilla, groin, and/or neck. Skin tags can also develop in affected areas.
4. **Psychiatric manifestation:** Depression, Anxiety disorders
5. **Infertility or difficulties conceiving**
6. **Associated condition:** Obesity, Insulin resistance, Metabolic syndrome, Non-alcoholic fatty liver disease

Note: Features associated with PCOS (e.g., obesity, Hyperandrogenism, difficulties conceiving) can have a negative psychosocial impact. If symptoms of anxiety and/or depression are identified, further mental health assessment and a referral to a mental health professional should be offered to the patient.



TREATMENT GUIDELINES OF PCOS

Recommendations for all PCOS patients

- » Encourage exercise and healthy eating (especially through caloric restriction), and consider behavioral strategies and modifications (setting goals, eating more slowly)
- » **Weight loss:** if patient is overweight ($BMI \geq 25 \text{ kg/m}^2$), target $BMI < 25 \text{ kg/m}^2$ can reduce estrone production by the adipose tissue.
- » Screen for comorbidities and provide specific treatment.
- » **Tailor additional therapeutic interventions based on:**
 - » Reproductive goals
 - » Comorbidities
 - » Individual risk factors

Treatment of PCOS for the patients not planning to conceive

For patients who do not wish to conceive, the therapeutic goals are to control menstrual irregularities and hyperandrogenism, treat comorbidities, and improve quality of life.

1. Combined oral contraceptives pills (COCs)

- » **Indication:** **First-Line Treatment** for hyperandrogenism and/or menstrual cycle abnormalities
- » **Additional benefits:** ↓ Endometrial hyperplasia → reduced risk of endometrial carcinoma, decreases Menstrual bleeding, decreases Acne, Treatment of hirsutism

2. Tab. Metformin (Glucophage): Improves menstrual irregularities, metabolic outcomes, and weight loss (especially when combined with lifestyle modifications)

- » **Second-Line Treatment** for menstrual irregularity in patients unable to take or tolerate COCPs
- » May be added to COCPs and lifestyle modification to improve metabolic outcomes

3. Antiandrogens: controversial role

- » **Drugs:** Tab. Spironolactone (Aldactone), Tab. Finasteride (Genesis), Tab. Flutamide (Flutamide)
- » **Indications:** can be considered for treatment of hirsutism and androgen-related alopecia in patients unable to take or tolerate COCPs
- » **Additional recommendation:** When using Antiandrogens as an alternative to COCPs, it is advisable to use other forms of contraception.

Treatment of PCOS for the patients planning to conceive

The goals of treatment for patients who wish to conceive are management of comorbidities (e.g., weight loss for overweight or obese patients) and induction of ovulation

1. Tab. Letrozole: first-line therapy for ovulation induction

- » Improves pregnancy and live birth rates in patients with anovulatory infertility with no other causes
- » **Mechanism of action:** aromatase inhibition reduces estrogen production, stimulating FSH secretion and inducing ovulation

2. Tab. Clomiphene citrate: alternative to letrozole

- » May be preferred over metformin monotherapy in obese women with anovulatory infertility
- » **Mechanism of action:** inhibits hypothalamic estrogen receptors → disruption of the negative feedback mechanism governing estrogen production → Increased pulsatile secretion of GnRH → ↑FSH and ↑LH → stimulation of ovulation

3. Exogenous gonadotropins (see below drug brand portion): The low-dose regimen is the second-line treatment for ovulation induction.

- » **Agents:** Exogenous FSH and human menopausal gonadotropin
- » **Indication:** Typically used if first-line therapies are unsuccessful; occasionally used as first-line if the drug and monitoring requirements are accessible

4. Tab. Metformin (Glucophage)

- » Can be used as second-line monotherapy for fertility treatment.
- » Combination with clomiphene may increase pregnancy rates, especially in obese women.
- » First-line therapy for insulin resistance



5. **Additional fertility interventions**
 - » **Laparoscopic ovarian drilling:** in this procedure ovarian tissue is reduced with a laser beam or surgical needle to decrease its volume and androgen production. This hormonal shift can induce FSH secretion and improve ovarian function in patients with polycystic ovary syndrome. **Second-line** treatment for ovulation induction, can damage ovary, doesn't resolve overall hormonal imbalance
 - » **In vitro fertilization:** can be offered as **third-line** therapy
 - » **Bariatric surgery:** no evidence of benefit in the treatment of infertility
6. **Management of other PCOS manifestations**
 - » **Hirsutism:** Non-pharmacological therapy is the first line treatment such as Electrolysis, light-based hair removal via laser or photoepilation.
 - » **Acne:** Consider topical therapies (Benzoyl peroxide and topical antibiotics)



TREATMENT OF PCOS – PATIENTS NOT PLANNING TO CONCEIVE

1. **Life-style modifications:** regular exercise, weight loss, healthy diet and control risk factors.
2. **Combined oral contraceptives (COCs)**
 - » **Tab. Ethinyl Estradiol 0.02mg + Drospirenone 3mg** (Tab. Yaz)
OR **Tab. Ethinyl estradiol 0.03mg + Levonorgestrel 0.15mg + Ferrous Fumarate 75mg** (Tab. Famila-28F, Tab. Novodol)
OR **Tab. Cyproterone Acetate 2mg + Ethinylloestradiol 35mcg** (Tab. Diane-35, Tab. Divestra)
Start from 1st day of periods and continue it according to instruction over the pack x once daily
21 days according to cycle then leave for 7 days
Duration: 3-6 months
 - » **Second-line treatment for menstrual irregularity in patients unable to take or tolerate COCs**
» **Tab. Metformin 500mg or 850mg** (Glucophage, Neophage) x Twice daily
3. **For Acne:** Benzoyl peroxide + clindamycin topical gel (Duac gel, Benclin Gel) x twice daily
4. **For Facial hairs/Hirsutism:** Non-pharmacological therapy is first line treatment such as Electrolysis, light-based hair removal via laser or photoepilation.
± Eflornithine Cream (Depilus, Eflogen) x apply once/twice daily on facial hair



TREATMENT OF PCOS – PATIENTS PLANNING TO CONCEIVE

1. **Life-style modifications:** regular exercise, weight loss, healthy diet and control risk factors
2. **First-line therapy for ovulation induction:** **Tab. Letrozole 2.5mg** (Femara, Lets, Letocor) at dose 2.5mg to 5mg x OD from the 2nd to 6th day of cycle. Ovulation should occur between days 14 to 19 (so please have intercourse beginning around day 12 and don't skip two days in a row through at least day 20). In the first cycle of Letrozole, you should have a blood progesterone level drawn 5-7 days after ovulation. If you get an excellent response from Letrozole (ovulation and excellent progesterone level) we'll continue Letrozole for 3-4 cycles.
Alternative to Letrozole
Tab. Clomiphene Citrate 50mg (Clomid, Ovafin, Ovi-F)
Start according to menstrual cycle in between day 3rd to day 7th of menstrual cycle x once daily
3. **Tab. Metformin 500mg or 850mg** (Glucophage, Neophage) at dose 500 – 850mg twice daily
» Combination of Tab. Clomiphene 50mg and Tab. Metformin 500mg might increase pregnancy rates
4. **Dietary Supplement: Myo-Inositol + Folic acid** (Slix, Myofolic, Inofolic, Inofer plus)
» Use once or twice daily, Dissolve contents in a glass of water (200 mL)

OVARIAN CYST (BENIGN)



Definition: An ovarian cyst is a fluid-filled structure/sac that may be simple or complex. The causes may be physiologic, infectious, benign neoplastic, malignant neoplastic, or metastatic. They are common findings usually discovered incidentally on physical examination or imaging.

Risk factors: Premenopausal age group early menarche, first trimester of pregnancy, personal history of infertility or polycystic ovary syndrome (Patients treated with gonadotropins or other ovulation induction agents may develop cysts as part of ovarian hyperstimulation syndrome.), increased intrinsic or extrinsic gonadotropins, tamoxifen therapy, hypothyroidism, personal or family history of endometriosis, smoking and tubal ligation

Classical complications: Rupture, Hemorrhage, Torsion

Δ Ovarian Cyst (Benign)

- Heaviness in the lower abdomen
- Bloating and early satiety
- Swelling
- Pelvic pain: Sharp or Dull
- Palpable adnexal mass

Diagnostic workup

Transvaginal ultrasound (TVUS):

- Enlarged ovary or portion of ovarian tissue; may be cystic, solid, or mixed, size <10cm, Septation Unilocular
- Findings that raise the level of suspicion for malignancy include cyst size >10 cm, presence of ascites, papillary excrescences or solid components, irregularity, and high color doppler flow.
- Pregnancy test (UPT): to exclude pregnancy

- Laparoscopy: This is of help to differentiate a painful cystic mass with disturbed ectopic pregnancy.
- Serum CA-125: To check in women with cysts suspicious for malignancy and all postmenopausal women. Serum CA-125 Levels >35 U/mL in postmenopausal women warrant concern for ovarian cancer.
- Tumor marker: Alpha-fetoprotein, beta-HCG, LDH, inhibin and Oestradiol (<40years female)



TREATMENT OF OVARIAN CYST (BENIGN) (First-line Prescription)

- Monitored conservatively with serial TVUS since the majority of cysts resolve spontaneously on their own without treatment
- If a cyst does not resolve after several menstrual cycles, it is unlikely to be a functional cyst, & further workup is indicated.
- **Maintain healthy lifestyle**
 - » Regular Exercise for 20-30 min
 - » Use healthy food, green vegetables, salad, fruits
 - » Increase intake of water and fresh juice intake
 - » Less use of fatty foods
 - » Avoid/no use broiler chicken, cold drinks, junk food

1. **Tab. Multivitamins** (Surbex-z, Revital Multi) x OD
2. **Tab. Ciprofloxacin 500mg** (Novidat, Cipesta, Ciproxen) x BD
OR **Cap. Cefixime 400mg** (Cefim, Cefiget, Cefspan) x OD
OR **Tab. Azithromycin 500mg** (Azitma, Zetro, Azomax) x OD
- If abdominal pain/spasm** (Anafortan Plus, Spasrid, Spasfon)
3. **Tab. Phloroglucinol + Trimethylphloroglucinol** x BD/TDS

FOLLICULAR CYSTS

Introduction: Follicular cysts are the most common functional cysts. They are usually multiple and small as seen in cases of cystic glandular hyperplasia of the endometrium or in association of fibroid. Hyperestrinism is implicated as its cause. However, an isolated cyst maybe formed in unruptured Graafian follicle, which may be enlarged but usually not exceeding 5 cm. The cyst is lined by typical granulosa cells without lutein cells or the cells may be flattened due to pressure

Diagnosis: In majority of cases, the detection is made accidentally on bimanual examination, sonography, laparoscopy or laparotomy. The cyst may remain asymptomatic or may cause vague pain.

Management of follicular cyst

- A follicular cyst ≤3 cm requires no further investigations.
- A simple cyst <7 cm, unilocular, echo free without solid areas or papillary projections, with normal serum CA-125 should be followed up with repeat TVUS in 3-6 months.
- COCs suppresses the levels of gonadotropins. Thereby reduces the stimulatory effects on the ovaries and the cysts. Low vascular resistance on color flow Doppler study suggests malignancy whereas high resistance usually suggests normal or benign disease.
- A cyst in a perimenopausal or postmenopausal women should be removed when serum CA 125 is abnormal (>35 IU/mL) or the cyst is persistently large (>10 cm). Removal (cystectomy) may be done by laparotomy or laparoscopy.



TREATMENT OF FOLLICULAR CYSTS

- **Ethinyl estradiol 0.03mg + Levonorgestrel 0.15mg + Ferrous Fumarate 75mg** (Tab. Familia-28F, Tab. Novodol)
- OR **Ethinyl Estradiol 0.02mg + Drospirenone 3mg** (Tab. Yaz)
- Start from 1st day of periods and continue it according instruction over the pack.
- **Duration:** 2-3 months



POSTPARTUM HEMORRHAGE (PPH)

- ☛ **Definition:** PPH is defined as estimated blood loss (EBL) > 500 mL for a vaginal delivery or > 1,000 mL for a cesarean delivery; or 10% drop in hematocrit (Hct) between admission and the postpartum period.
- ☛ **Classification:**
 - » **Primary PPH (Early):** Most common, blood loss after birth of the baby up to 24 hours of delivery.
Causes (4T's): **T**one (Uterine atony), **T**issue (retained products of conception), **T**rauma to genital tract (Laceration, hematoma, inversion, Rupture) and **T**hrombin (DIC, coagulopathies)
 - » **Secondary PPH (Late):** Blood loss from 24 hours to 6 weeks after delivery
Causes: usually due to infection (endometritis), retained product of conception, abnormal placentation.
- ☛ **Clinical Presentation:**
 - » Rapid, heavy vaginal bleeding
 - » Possible signs of hypovolemia/blood loss (decreased BP, Increased heart rate, dizziness)
- ☛ **Complications of PPH:** Anemia, hypovolemic shock, thromboembolism, sheehan syndrome, infection, maternal death, fetal death (velamentous cord insertion), abdominal compartment syndrome
- ☛ **Diagnostic workup:**
 - » **Laboratory measure:** CBC = Hematocrit, Hb to estimate blood loss, coagulation profile
 - » **Physical exam findings:** e.g., lacerations, hematoma, any other visible cause of bleeding, boggy uterus
 - » **Speculum exam to diagnose the following:** Uterine inversion, Retained placental tissue or membranes
 - » **Ultrasound (Abdomen/Pelvic):** Used to determine the correlation between the placenta and the cervical os
Helpful to diagnose the following:
 - ↳ **Uterine atony:** showing, e.g., an echogenic endometrial stripe.
 - ↳ **Abnormal placental attachment:** showing, e.g., thinning of uterine myometrial wall
 - » **Color Doppler ultrasound:** to confirm abnormal placental attachment (showing, e.g., turbulent blood flow)



TREATMENT OF POSTPARTUM HEMORRHAGE (PPH)

- ☛ Establish large-bore intravenous (IV) line (18-gauge or larger).
- ☛ **Vitals monitoring:** BP, PR, RR, Temperature, Check SpO₂ and administer supplemental O₂ as appropriate.
- ☛ **Start IV fluid therapy with crystalloids:** 0.9% normal saline or Ringer lactate.
- ☛ **Fluid monitoring:** Aim for urinary output of 30 mL/hour or more
- ☛ **Obtained investigations:** CBC, Urea, Creatinine and Electrolytes, Coagulation profile.
- ☛ **Initial Interventions**
 - » **Uterine Massage:** Perform bimanual uterine massage to stimulate uterine contractions.
 - ↳ A clenched fist is inserted into the anterior vaginal fornix and exerts pressure on the anterior wall of the uterus.
 - ↳ The other hand is positioned externally and presses against the inner fist, located in the uterine body.
 - i. **Fritsch maneuver**
 1. One hand grasps the labia majora and presses it firmly into the vulva.
 2. Simultaneously, the second hand is positioned at the posterior side of the uterus (as in Credé maneuver) and is pushed distally against the other hand.
 3. The placenta is manually removed.
 4. Fundal massage
 - ii. **Credé maneuver**
 1. The cranial part of the uterus is held with four fingers positioned at the posterior side of the uterus and the thumb at the anterior surface.
 2. The pressure compresses the uterine vessels and aids in the expulsion of the placenta.
 3. Avoidance of unnecessary episiotomy and instrumented delivery
 - » **Administer Uterotonic drugs:**
 - » **Inj. Oxytocin 5 I.U./1ml (Syntocinon)** x 5-10 I.U IV over 1-2 minutes or IM and at a same time 30-40 I.U in 500 ml of crystalloid (0.9% NS or R/L) administered at the rate of 125mL/hour (or 160 drops per minutes).



- OR Tab. Misoprostol 200mcg (Cytotec, Breeky) at dose 600–1000mcg x per rectally (first line), per oral or sub-lingual (second line), if oxytocin is unavailable.
- OR Inj. Methyl-Ergometrine 0.2mg/1ml (Methergine) at dose 0.2mg x IM every 2 to 4 hours (maximum 5 doses) or IV diluted in upto 5ml of 0.9% NS over 1–2 minutes, contraindicated in hypertension.
- OR Inj. Carboprost tromethamine 250mcg/ml (Hemabate) at dose 250 mcg IM every 15–90 minutes (maximum 8 doses), contraindicated in asthma.

Remember: Initially for PPH, oxytocin or Ergometrine (Methergin) is given. If it fails to control the bleeding, then 15 methyl PGF_{2a} or Misoprostol is given. Repeat dose not recommended.

Identify and treat the cause of hemorrhage

1. **Check for uterine atony:** Continue uterotonic therapy and uterine massage.
2. **Evaluate for trauma:** Inspect for vaginal, cervical, or perineal lacerations and repair as needed.
 - **Controlled umbilical cord traction** (Brandt-Andrew's maneuver)
 - One hand is placed on the abdomen, securing the uterine fundus and preventing uterine inversion.
 - The other hand applies steady downward traction on the umbilical cord.
 - **Avoidance of unnecessary episiotomy and instrumented delivery**
3. **Assess for retained placental tissue:** Perform a manual exploration of the uterus if needed to remove any retained tissue.

Manual removal of placenta

- Consider administering nitroglycerin.
- Perform under adequate regional or general anesthesia.
- Administer prophylactic antibiotics.
- **Technique**

1. Keep fingers tightly together and use the edge of the hand to make a space between the placenta and the uterine wall to detach the placenta completely.
2. After placenta is detached, withdraw the hand from the uterus, bringing the placenta with it.
3. With the other hand, perform countertraction to the fundus by pushing it in the opposite direction of the hand that is removing the placenta.

4. **Investigate for coagulopathy:** Draw blood for CBC, coagulation profile, blood grouping and crossmatch.
 - Blood transfusion should be considered after 1–2L EBL.
 - Coagulation factors (FFP and coprecipitate) and platelets should be repleted with massive blood loss. One unit of FFP is given for every 4–6 units of packed RBC to reduce dilutional and citrate coagulopathy. Consider platelet transfusion as the platelet count drops below 50,000/ μ L.
 - **Inj. Tranexamic acid 500mg/5ml** (Transamin) **at dose** 1g, undiluted x IV STAT over 10 minutes, if bleeding persists after 30 minutes or stops and restarts within 24 hours of the first dose, a second dose may be administered. Should be given as soon as possible after bleeding onset to stop fibrinolysis and reduce the likelihood of mortality

- **Antibiotics for Secondary infection:** Inj. Ceftriaxone 2g (Oxidil, Titan) x IV x OD, diluted in 100ml 0.9% NS.
- **Gastro protective:** Inj. Esomeprazole 40mg/vial (Nexum, Eskem), diluted in 100ml 0.9% NS x IV

Advanced Interventions

- **Balloon Tamponade:** Insert a Bakri balloon or similar device to tamponade the uterus, if severe bleeding persists, regardless of adequate general measures
- **Uterine Packing:** Use gauze or other materials to pack the uterus if a balloon tamponade is not available or effective.

Surgical treatment

- Dilation and curettage (D&C) to remove retained placental tissue.
- Surgical ligation of uterine or internal iliac arteries
- B-Lynch suture or other compression sutures.
- **Last resort:** Hysterectomy as a last resort if all other measures fail.

Post-Hemorrhage Care

- Monitor for signs of infection, anemia, or other complications related to PPH.
- **Provide Emotional Support:** Offer psychological support and counseling to the patient and family.



NAUSEA & VOMITING IN PREGNANCY (NVP)

- ☞ **Definition:** Nausea and vomiting in pregnancy (NVP), commonly referred to as morning sickness, affects approximately 75% of pregnant women, begins between the 4th & 8th week after the last menstrual period. It is characterized by nausea and vomiting that occur more frequently during the morning hours, and typically resolves in the second trimester.

Rx

TREATMENT OF NAUSEA & VOMITING IN PREGNANCY (NVP)

- ☞ Rehydration (oral hydration is usually sufficient)
- ☞ Adapt diet and avoid triggers.
- ☞ Advice Ginger (*Zingiber officinale*) tea, if patient unable to take anti-emetics x 4-5 times a day
- ☞ Replace iron-containing supplements with folate-containing prenatal vitamins (Tab. Myfol 400mcg x OD)
- ☞ **Antiemetic therapy for nausea and vomiting of pregnancy:** If the response to an antiemetic from one class is inadequate, add an antiemetic from another class in a stepwise manner, as shown below.
 1. Tab. Doxylamine 10mg + Vitamin-B6 10mg (Envepe, Femiroz) x TDS/BD
OR Tab. Meclizine 25mg + Vitamin-B6 50mg (Navidoxine) x BD
 2. For refractory symptoms despite combination therapy above, add one of the following anti-emetic:
 - ☞ Tab. Dimenhydrinate 50mg (Gravinate) x TDS
OR Tab. Metoclopramide 10mg (Maxolon, Metoclon) x TDS
OR Tab. Ondansetron 8mg (Onset, Onseron) x 4 to 8mg x BD/TDS
OR Tab. Prochlorperazine 5mg (Stemetil) x TDS
OR Tab. Promethazine 25mg (Avomine) x TDS
 - ☞ Consider also: Change oral Dimenhydrinate (Gravinate) to IV Gravinate.
 3. Last resort: Add corticosteroids (methylprednisolone see Hyperemesis Gravidum)
 4. IV fluid: Inj. Ringer Lactate 500ml – 1L + Inj. Neurobion 2ml x IV x STAT

HYPEREMESIS GRAVIDARUM (HG)

Definition: Hyperemesis gravidarum is the most severe form of Nausea and vomiting in pregnancy (NVP) and is characterized by persistent vomiting, dehydration, ketosis, electrolyte imbalance, and weight loss.

Rx

TREATMENT OF HYPEREMESIS GRAVIDARUM (HG)

- ☞ Admit the patient (Inpatient admission) → Consult OB/GYN
- ☞ **IV fluid resuscitation/replacement:** Start IV fluids containing Dextrose 5%, Ringer lactate or Normal saline to replete volume and reverse ketonuria.
- ☞ **Lab:** Electrolyte disturbances (hypokalemia & hypochloremic metabolic alkalosis), CBC – (normal or hematocrit ↑), urinalysis (Ketonuria – urine ketone 2+), Serum urea and creatinine (variable; elevated)
- ☞ **IV Electrolyte repletion:** if ↓ K⁺ add 25ml KCL in 1L NS or calculate deficit
- ☞ **IV Thiamine repletion (Inj. Neurobion),** consider in patient with severe recurrent vomiting, better add in R/L
- ☞ **IV Antiemetic Therapy**
 - » Inj. Dimenhydrinate 50mg (Gravinate) x IV x TDS OR Inj. Metoclopramide 10mg (Metaclon) x IV x TDS
 - » If fail: Inj. Ondansetron 8mg (Onset) 4 – 8mg x IV in 20 – 30 ml NS over 10-15 minute x BD/TDS
 - » If fail: Consider corticosteroids – Inj. Hydrocortisone 100mg x IV x BD OR Inj. Methylprednisolone 16mg x IV x three time daily for 3 days once improvement occurs, than convert it to Tab. Prednisolone 5mg (Deltacortril, Rapicort) at dose 40-60mg daily per orally once or twice, with the dose gradually tapered down until the lowest maintainance dose that controls the symptoms is reached.
- ☞ **Proton-pump inhibitors (PPIs):** Inj. Esomeprazole 40mg (Esso, Nexum) x IV once daily
- ☞ Consider enteral tube feeding (Nasogastric/nasoduodenal) or TPN.
- ☞ Closely monitor vitals and urine output. Monitor urine ketones, BUN/Urea, creatinine, electrolytes, and BMI.
- ☞ Check other co-morbidities that causes severe nausea/vomiting



NAUSEA & VOMITING IN PREGNANCY (NVP)

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Rx

TREATMENT OF NAUSEA & VOMITING IN PREGNANCY (NVP)

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- ☞ Adapt diet and avoid triggers.
- ☞ Advice Ginger (*Zingiber officinale*) tea, if patient unable to take anti-emetics x 4-5 times a day
- ☞ Replace iron-containing supplements with folate-containing prenatal vitamins (Tab. Myfol 400mcg x OD)
- ☞ **Antiemetic therapy for nausea and vomiting of pregnancy:** If the response to an antiemetic from one class is inadequate, add an antiemetic from another class in a stepwise manner, as shown below.
 1. Tab. Doxylamine 10mg + Vitamin-B6 10mg (Envepe, Femiroz) x TDS/BD
OR Tab. Meclizine 25mg + Vitamin-B6 50mg (Navidoxine) x BD
 2. For refractory symptoms despite combination therapy above, add one of the following anti-emetic:
 - ☞ Tab. Dimenhydrinate 50mg (Gravinate) x TDS
 - OR Tab. Metoclopramide 10mg (Maxolon, Metoclon) x TDS
 - OR Tab. Ondansetron 8mg (Onset, Onseron) x 4 to 8mg x BD/TDS
 - OR Tab. Prochlorperazine 5mg (Stemetil) x TDS
 - OR Tab. Promethazine 25mg (Avomine) x TDS
 - ☞ Consider also: Change oral Dimenhydrinate (Gravinte) to IV Gravinate.
 3. Last resort: Add corticosteroids (methylprednisolone see Hyperemesis Gravidum)
 4. IV fluid: Inj. Ringer Lactate 500ml – 1L + Inj. Neurobion 2ml x IV x STAT

HYPEREMESIS GRAVIDARUM (HG)

Definition: Hyperemesis gravidarum is the most severe form of Nausea and vomiting in pregnancy (NVP) and is characterized by persistent vomiting, dehydration, ketosis, electrolyte imbalance, and weight loss.

Rx

TREATMENT OF HYPEREMESIS GRAVIDARUM (HG)

- ☞ Admit the patient (Inpatient admission) → Consult OB/GYN
- ☞ **IV fluid resuscitation/replacement:** Start IV fluids containing Dextrose 5%, Ringer lactate or Normal saline to replete volume and reverse ketonuria.
- ☞ **Lab:** Electrolyte disturbances (hypokalemia & hypochloremic metabolic alkalosis), CBC – (normal or hematocrit ↑), urinalysis (Ketonuria – urine ketone 2+), Serum urea and creatinine (variable; elevated)
- ☞ **IV Electrolyte repletion:** if ↓ K⁺ add 25ml KCL in 1L NS or calculate deficit
- ☞ **IV Thiamine repletion (Inj. Neurobion),** consider in patient with severe recurrent vomiting, better add in R/L
- ☞ **IV Antiemetic Therapy**
 - » Inj. Dimenhydrinate 50mg (Gravinate) x IV x TDS OR Inj. Metoclopramide 10mg (Metaclon) x IV x TDS
 - » If fail: Inj. Ondansetron 8mg (Onset) 4 – 8mg x IV in 20 – 30 ml NS over 10-15 minute x BD/TDS
 - » If fail: Consider corticosteroids – Inj. Hydrocortisone 100mg x IV x BD OR Inj. Methylprednisolone 16mg x IV x three time daily for 3 days once improvement occurs, then convert it to Tab. Prednisolone 5mg (Deltacortril, Rapicort) at dose 40-60mg daily per orally once or twice, with the dose gradually tapered down until the lowest maintainance dose that controls the symptoms is reached.
- ☞ **Proton-pump inhibitors (PPIs):** Inj. Esomeprazole 40mg (Esso, Nexum) x IV once daily
- ☞ Consider enteral tube feeding (Nasogastric/nasoduodenal) or TPN.
- ☞ Closely monitor vitals and urine output. Monitor urine ketones, BUN/Urea, creatinine, electrolytes, and BMI.
- ☞ Check other co-morbidities that causes severe nausea/vomiting

CHRONIC HYPERTENSION IN PREGNANCY



- Chronic hypertension in pregnancy is defined as a systolic BP of ≥ 140 mmHg or a diastolic BP of ≥ 90 mmHg that diagnosed before pregnancy or in the first 20 weeks of pregnancy with or without end-organ dysfunction.
- Severe chronic hypertension is systolic BP > 160 mmHg or diastolic BP > 110 mmHg.
- Women with chronic hypertension are at increased risk for placental abruption, preeclampsia, low birth weight, cesarean delivery, premature birth, and fetal demise.
- Presentation: usually asymptomatic. Nonspecific symptoms (morning headaches, fatigue, and dizziness) can occur.

TREATMENT OF CHRONIC HYPERTENSION IN PREGNANCY

- All patients: Encourage lifestyle modifications for hypertension $\rightarrow$ salt restriction of ≤ 2.4 g/day. Dietary modifications with increased fruits and vegetables and decreased total and saturated fats can be encouraged. Smoking and alcohol cessation. Mild activity restrictions, due to concern for decreased uteroplacental blood flow increasing risk of preeclampsia. Dieting and weight loss are not advised in pregnancy, even for obese women.
- Threshold to initiate antihypertensives (in treatment-naïve patients): Blood pressure $\geq 140/90$ mmHg
- Target blood pressure
 - Titrate antihypertensives to maintain blood pressure between 120/80 mmHg and 140/90 mmHg.
 - Lower blood pressure targets may be appropriate in patients with comorbidities (e.g., diabetes mellitus, renal dysfunction); consult specialists for optimal management.
- Suspected secondary hypertension: Refer for specialist management
- Antihypertensives therapy for Lowering blood pressure (BP)

- In patient with mild to moderate hypertension: BP 140/90 mmHg to 159/109 mmHg
 - Tab. Labetalol 100mg (Labetolol) at dose 100mg orally twice daily initially, increase gradually according to response, usual dose 100-400 mg twice daily, maximum 2400 mg/day.
 - OR Tab. Nifedipine (Adalat LA 30mg, Adalat LA 60mg) at dose 30-60 mg (extended-release) orally once daily initially, increase gradually according to response, maximum 90-120 mg/day.
 - OR Tab. Methyldopa 250mg (Aldomet) at dose 250mg orally 2-3 times daily initially, increase gradually according to response, usual dose 250-1000 mg/day given in 2-4 divided doses, maximum 3000mg/day
- Methyldopa should be avoided in the postpartum period because of its association with depression; women already taking methyldopa should change to an alternative antihypertensive treatment within 2 days of delivery. Side effects: Hepatic injury, should be monitored LFTs at least once per trimester.
- OR Tab. Hydralazine 25mg (Zafa Pharma) at dose 10 – 25mg twice daily
- In patient with severe hypertension (Hypertensive crisis): BP $\geq 160/110$ mmHg
 - Step-1: Inj. Labetalol 50mg/10ml (Labetolol – Zafa Pharma) at dose 20 mg IV initially, followed by 40mg if BP threshold is still exceeded after 10 minutes, followed by 80 mg if BP threshold is still exceeded after 10 minutes.
 - Step-2: Switch to hydralazine if BP threshold is still exceeded/target BP not achieved after 10 minutes
 - Inj. Hydralazine 20mg/1ml x at dose 5 – 10mg IV initially, followed by 10 mg if BP threshold is still exceeded after 20 minutes; switch to labetalol if BP threshold is still exceeded after 20 minutes.
 - Step-3: Tab. Nifedipine 10 mg (Adalat LA 30mg, Adalat LA 60mg) at dose 30-60mg (extended-release) orally once daily initially, followed by 20mg if BP threshold is still exceeded after 20 minutes, followed by 20 mg if BP threshold is still exceeded after 20 minutes; switch to labetalol if BP threshold is still exceeded after 20 minutes and consult specialist for further guidance on dose protocol.

Thiazide diuretics — inhibit renal sodium and chloride reabsorption. A large meta-analysis found no adverse outcomes in pregnancy, however decreased plasma volume from diuresis carries a theoretic risk of placental insufficiency, which deters its use as first-line agent. The initial dose of Hydrochlorothiazide (HCTZ) is 12.5 to 25mg daily, titrated every 2 to 3 weeks to a maximum dose of 50mg/day. Diuretics are not recommended in the setting of preeclampsia, uteroplacental insufficiency, or IUGR. Serum uric acid increases with thiazide diuretics, limiting diagnostic options for preeclampsia. Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) are not recommended in pregnancy due to severe fetal malformations and neonatal renal failure, pulmonary hypoplasia, and fetal death.

References: NICE Guidelines, RCOG, The FIGO Textbook of Pregnancy Hypertension (2016) p142, The John Hopkins Manual of gynae & Obst 4th ed.



PRE-ECLAMPSIA

Clinical features

Preeclampsia without severe features	Preeclampsia with severe features
» Usually asymptomatic » Nonspecific symptoms may include: ▪ Headache ▪ Problems with vision, such as blurring or flashing ▪ Severe pain just below the ribs ▪ Vomiting ▪ Sudden swelling of the face, hands or feet. » Hypertension (BP $\geq 140/90$ mmHg). » Proteinuria.	» Severe hypertension (BP $\geq 160/110$ mmHg) » Oliguria: 24-hr urine output < 500 mL » Severe Headache » Proteinuria » Visual disturbances (blurred vision, scotoma) » RUQ pain or epigastric pain » Pulmonary edema » Cerebral symptoms (Altered mental status, nausea, vomiting, hyperreflexia, clonus)

DIAGNOSTIC APPROACH

History taking and physical examination

- » **Onset:** occurs in women after 20 weeks' of gestation. In 90% cases occur after 34 weeks' of gestation.
- » **Blood pressure:** $\geq 140/90$ mmHg (defined as systolic BP ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg) in a previously normotensive woman is diagnostic. At least **TWO** measurements should be made, at least 4 hours apart. Considered severe if systolic BP ≥ 160 mmHg and/or diastolic BP ≥ 110 mmHg.
- » **Headache:** Usually frontal headache. Presence of this symptom classifies preeclampsia as severe
- » **Right upper quadrant pain:** Occurs in around 16% of women with severe disease, and is a clinical symptom of **HELLP syndrome** (Hemolysis, Elevated Liver enzymes and Low Platelets syndrome).
- » **Ophthalmoscopic examination:** In severe cases there may be retinal edema, constriction of the arterioles, alteration of normal ratio of vein: arteriole diameter from 3:2 to 3:1 and nicking of the veins where crossed by the arterioles. There may be hemorrhage.
- » **Antenatal fetal monitoring:** Antenatal fetal wellbeing assessment is done by clinical examination, daily fetal kick count, ultrasonography for fetal growth and liquor pockets, cardiotocography, umbilical artery flow velocimetry and biophysical profile

Obtain investigation: CBC, LFTs, Uric acid, Urea, creatinine, coagulation profile and urinalysis

- » **Urinalysis:** $\uparrow$ Proteinuria is diagnostic, there may be few hyaline casts, epithelial cells or even few red cells.
- » **CBC:** Platelet count: $\leq 100,000/\mu\text{L}$. Hematocrit (Hct) level $\downarrow$ secondary to severe hemolysis in HELLP syndrome.
- » **Serum uric acid level:** $\uparrow$ (≥ 5 mg/dL) - indicates the presence of pre-eclampsia.
- » **Serum creatinine:** $\uparrow$ (≥ 1.2 mg/dL), creatinine normally $\downarrow$ in pregnancy, so even slight $\uparrow$ warrant severity.
- » **LFTs:** deranged ALT, AST, LDH
- » **Coagulation profile** is not necessary when platelet count and LFTs are normal. Prolonged PT & APTT may be due to primary coagulopathy, hepatic synthesis dysfunction, or abruptio placentae leading to DIC.

DIAGNOSTIC CRITERIA FOR PRE-ECLAMPSIA

Gestational hypertension: Hypertension (BP $\geq 140/90$ mmHg) diagnosed at ≥ 20 weeks' gestation (Prior to 20 weeks' gestation, patients were normotensive at all previous prenatal care visits, No history of preexisting hypertension).

Preeclampsia without severe features	PREECLAMPSIA WITH SEVERE FEATURES
» Hypertension ($\geq 140/90$ mm Hg) » And proteinuria, as evidenced by any of the following: ▪ 24-hour urine collection: ≥ 300 mg/24 hours ▪ Urine protein: creatinine ratio: ≥ 0.3 ▪ Urine dipstick: $> 2+$ protein	- Gestational hypertension, plus ≥ 1 of the following: » Severe hypertension (systolic BP ≥ 160 mmHg or diastolic BP ≥ 110 mmHg) » Thrombocytopenia: platelets $< 100,000$ cells/mm³ » Impaired renal function: Serum creatinine > 1.1 mg/dL Or doubling of serum creatinine » Impaired LFT not explained by alternative diagnoses: ▪ ≥ 2 times the ULN of transaminases (ALT, AST) ▪ Severe, refractory RUQ or epigastric pain » Pulmonary edema » New onset of either: » Headache that is unresponsive to medication » Visual disturbances: blurred vision, scotoma
HELLP SYNDROME	
Preeclampsia plus all of the following: » H = Hemolysis (e.g., $\downarrow$ hemoglobin, $\downarrow$ haptoglobin, $\uparrow$ LDH, and $\uparrow$ indirect bilirubin) » EL = Elevated Liver enzymes ($\uparrow$ AST, $\uparrow$ ALT) » LP = Low Platelets ($< 100,000$ cells/mm³).	

TREATMENT OF PRE-ECLAMPSIA

- Hospital admission and monitoring:** Women with clinical findings that warrant close attention should be managed in an **inpatient care facility**. On admission, further assessment is required.
- BP should be monitored regularly at least 4 times per day.
 - In cases of well-controlled mild to moderate disease, outpatient treatment with oral hypertensive can be considered, although close outpatient monitoring in a day unit or equivalent is required.
 - Rest is helpful for continued evaluation and treatment of the patient. While in bed patient should be in left-lateral position as much as possible, to lessen the effects of vena caval compression.
 - Rest – (1) increases renal blood flow → diuresis, (2) increases uterine blood flow → improves placental perfusion, and (3) reduces the blood pressure. However complete bed rest is not essential.
 - Diet: The diet should contain adequate amount of daily protein (about 100g). Usual salt intake is permitted. Fluids need not be restricted. Total calorie approximate 1,600 cal/day.
 - Diuretics: The diuretics should not be used injudiciously, as they cause harm to the baby by diminishing placental perfusion and by electrolyte imbalance. → **Indication for diuretics use:** (1) Cardiac failure, (2) Pulmonary edema, (3) along with selective antihypertensive drug therapy (diazoxide group) where blood pressure reduction is associated with fluid retention, (4) massive edema, not relieved by rest and producing discomfort to the patient. The most potent diuretic commonly used is **Tab. Furosemide 40mg (Lasix)** at dose 20-40mg orally after breakfast for 5 days in a week. In acute condition, intravenous (iv) route is preferred.
 - Lowering blood pressure (BP) → **Antihypertensives therapy**
 - In patient with mild to moderate hypertension: BP 140/90 mmHg to 159/109 mmHg
 - Tab. Labetalol 100mg (Labetolol – Zafa Pharma) at dose 100mg orally twice daily initially, increase gradually according to response, usual dose 100-400 mg twice daily, maximum 2400 mg/day.
 - OR Tab. Nifedipine (Adalat LA 30mg, Adalat LA 60mg) at dose 30-60mg (extended-release) orally once daily initially, increase gradually according to response, maximum 90-120 mg/day.
 - OR Tab. Methyldopa 250mg (Aldomet) at dose 250mg orally 2-3 times daily initially, increase gradually according to response, usual dose 250-1000mg/day given in 2-4 divided doses, maximum 3000 mg/day. Methyldopa (Aldomet) should be avoided in the postpartum period because of its association with depression; women already taking methyldopa should change to an alternative antihypertensive treatment within 2 days of delivery.
 - OR Tab. Hydralazine 25mg (Zafa Pharma) at dose 10 – 25mg twice daily
 - In patient with severe hypertension (Hypertensive crisis): BP ≥160/110 mmHg
 - Step-1: Inj. Labetalol 50mg/10ml (Labetolol – Zafa Pharma) at dose 20 mg IV, undiluted initially, followed by 40 mg if BP threshold is still exceeded after 10 minutes, followed by 80mg if BP threshold is still exceeded after 10 minutes.
 - The escalating bolus protocol: Inj. Labetalol at dose 20mg followed by 40mg, if not effective within 10 min; then 80mg → 80mg → 80mg given at 10-min intervals, up to a max: of 300mg/24 hour
 - The continuous-infusion protocol: Starts at 0.5 mg/kg/hour and increases every 30 minutes by 0.5mg/kg/hour to a maximum dose of 3mg/kg/hour.
 - Step-2: Switch to hydralazine if BP threshold is still exceeded/target BP not achieved after 10 minutes
 - Inj. Hydralazine 20mg/1ml (Hydralazine – Zafa Pharma) x at dose 5 – 10mg IV initially, followed by 10 mg if BP threshold is still exceeded after 20 minutes; switch to labetalol if BP threshold is still exceeded after 20 minutes.
 - Step-3: Tab. Nifedipine 10mg (Adalat LA 30mg, Adalat LA 60mg) at dose 30-60mg (extended-release) orally once daily initially, followed by 20mg if BP threshold is still exceeded after 20 minutes, followed by 20mg if BP threshold is still exceeded after 20 minutes; switch to labetalol if BP threshold is still exceeded after 20 minutes and consult specialist for further guidance on dose protocol.
 - Progress chart: The effect of treatment should be evaluated by maintaining a chart – Records the following:
 - Daily clinical evaluation for any symptoms: e.g. headache, right upper quadrant abdominal or epigastric pain, visual disturbances, oliguria.
 - Blood pressure: 6 times a day with appropriate cuff size.
 - State of edema and daily weight record.



4. Input/output record: Fluid intake and urinary output.
5. Urine examination (urinalysis) for protein daily and if present, to estimate its amount in 24 hours urine.
6. Obtain CBC (Hct, platelet count), uric acid, creatinine, LFTs, coagulation profile at least once a week.
7. Ophthalmoscopic examination on admission and to be repeated, if necessary.
8. Fetal wellbeing assessment (DFMCR, NST, or BPP)

Favorable signs: In favorable cases, there is fall of blood pressure and weight with subsidence of edema. Urinary output increases with diminishing proteinuria, if previously present.

- **Magnesium sulphate for seizure prophylaxis for at least 24 hours:** Magnesium sulfate is recommended before 34 weeks' gestation for neuro-protection of the baby if women are in established preterm labor or having a planned preterm birth within 24 hours.

Inj. Magnesium sulfate 500mg/1ml (Zafa Pharma) at loading dose of 4–6 g IV in 100ml to 150ml 0.9% NS administered over 15 to 20 minutes. (A second loading dose of 2–4 g IV may be given for patients experiencing eclamptic seizures) followed by 1–2 g/hour IV infusion (25 ml/hour to 50 ml/hour).

- » **Magnesium sulfate (Mg So₄)** is contraindicated in patients with myasthenia gravis and should be administered with care in patients with renal insufficiency.
- » **Monitoring for magnesium toxicity (hypermagnesemia) for at least every 1-2 hours.**
 - ↳ Monitor all patient for clinical signs of magnesium toxicity → deep tendon (patellar) reflexes ↓, BP ↓, respiratory rate ↓ (respiratory depression), poor urine output (oliguria), slurred speech, Diaphoresis → stop magnesium and check serum magnesium levels
 - ↳ Administer **Inj. Calcium gluconate 10%/10ml (1g/10ml)** x IV over 3 minutes and consider diuretics (e.g., IV furosemide, IV mannitol).
- **Corticosteroids for fetal lung maturation:** If early birth is considered likely within 7 days in women with pre-eclampsia, offer a course of antenatal corticosteroids.
 - » **Inj. Betamethasone 4mg/1ml** (Betnesol) x 12mg x IM x OD for 2 days
 - » OR **Inj. Dexamethasone 4mg/1ml** (Decadron) x 6mg x IM x BD for 2 days.
- **IV fluid resuscitation:** In women with severe pre-eclampsia, limit maintenance fluids to 80 ml/hour R/L unless there are other ongoing fluid losses (for example, haemorrhage). Patients with preeclampsia are frequently hypovolemic due to third spacing from low serum oncotic pressure and increased capillary permeability.
- **Oliguria is defined as urine output of <100 mL in 4 hour.**
 - » Treated with IV crystalloid 500-mL bolus if the lungs are clear. If there is no response, another 500-mL bolus can be administered. If there is no response after 1L
 - » Central hemodynamic monitoring can be considered → Central venous pressure monitoring does not correlate well with pulmonary capillary wedge pressure. A Swan-Ganz catheter may be required to help guide fluid management and prevent flash pulmonary edema
- **Definitive treatment of pre-eclampsia is termination of pregnancy (delivery)** – As such, the aim of the above treatment is to continue the pregnancy, if possible, without affecting the maternal prognosis until the fetus becomes mature enough to survive in extrauterine environment (>37 weeks).

PATIENTS WITH PREECLAMPSIA WITH SEVERE FEATURES, HELLP, OR ECLAMPSIA

- **Initial maternal and fetal management**
 - » ABCD&E approach and Provide supplemental oxygen or mechanical ventilation as appropriate.
 - » Maintain intravenous (IV) access and Obtain routine blood test.
 - » Keep NPO until the management plan has been decided (emergency cesarean delivery may be required).
 - » Start continuous maternal and fetal monitoring.
 - » Consult obstetrics, maternal-fetal medicine, and critical care urgently.
 - » Admit or transfer to a tertiary care hospital; consider ICU admission.
 - » Initiate antihypertensives for urgent blood pressure control in pregnancy.
 - » **Seizure prophylaxis:** Administer magnesium sulfate for seizure prophylaxis.
 - » Administer IV fluid therapy and electrolyte repletion as needed.
 - » Consider blood products (e.g., platelets, PRBCs, FFP) as needed to manage hemorrhage and coagulopathy
 - » Manage end-organ failure (e.g., acute renal failure, acute liver failure, DIC) if present.
 - » Monitor vital signs closely and perform full obstetrical ultrasound.
 - » Assess for indications for immediate delivery regardless of gestational age.



- » Fetal management
 - » Indications for immediate delivery regardless of gestational age present: urgent delivery after maternal hemodynamic stabilization
 - » Indications for immediate delivery regardless of gestational age absent
 - » ≥ 34 weeks' gestation: Deliver.
 - » 24–34 weeks' gestation
 - » Administer corticosteroids for fetal lung maturity.
 - » Initiate serial monitoring (including non-stress test and biophysical profile) if expectant management is planned.
 - » Serially assess for indications for immediate delivery; if present, deliver immediately.
 - » Expedite delivery after administration of corticosteroids.
 - » Before fetal viability: Continuation of pregnancy is not recommended.
- » Intrapartum and postpartum management
 - » Serially monitor maternal vital signs and laboratory studies until normalized.
 - » Pain management: NSAIDs are preferred over opioids for analgesia.
 - » Continue magnesium sulfate for 24 hours after delivery.
 - » Continue antihypertensives; titrate dosage to maintain blood pressure within the normal range.

PROPHYLACTIC MEASURES FOR PREVENTION OF PREECLAMPSIA

Assess all patients with chronic hypertension and gestational hypertension for risk factors for preeclampsia.

HIGH-RISK FACTORS	MODERATE-RISK FACTORS
» Previous eclampsia or preeclampsia » Chronic hypertension » Diabetes mellitus type 1 or 2 » Autoimmune disease: » Antiphospholipid syndrome » Systemic lupus erythematosus (SLE) » Chronic kidney disease (CKD) » Multiple gestation (e.g., twins)	» First pregnancy » Mother age ≥ 35 years » Pregnancy interval of more than 10 years » Body mass index (BMI) of 30kg/m^2 » Gestational diabetes, and black individuals (Non-Hispanic) » Pregnancy risk factors: e.g., small for gestational age, history of poor pregnancy outcome, in vitro fertilization, interval between pregnancies ≥ 10 years)

» **Counselling:** Educate at-risk patients on the symptoms of preeclampsia. If preeclampsia does develop, management depends on the severity.

- » **Regular antenatal checkup** for early detection of rapid gain in weight or a tendency of rising blood pressure especially the diastolic one.
- » **Exercises:** Physical activity, stretching.
- » **Supplementation:** calcium 2g/day (reduces the risk of gestational hypertension), magnesium and zinc
- » **Antioxidants:** vitamins-C, vitamin-E and vitamin-D
- » **Diet:** Balanced diet rich in protein may reduce the risk, low-salt diet and fish oil

» **Aspirin for preeclampsia prophylaxis**

- » **Indications**
 - » Recommended in individuals with ≥ 1 high-risk feature or ≥ 2 moderate-risk factors for preeclampsia.
 - » Consider in individuals with 1 moderate-risk factor for preeclampsia.
- » **Prevention regimen**
 - » **Primary Prevention:** Low-dose aspirin (Ascard, Loprin) at dose 75–150 mg/day orally starting between 12 and 28 weeks' gestation, and optimally before 16 weeks' gestation, and continuing prophylaxis until the birth (delivery) of the baby reduces the incidence and severity of preeclampsia.
 - » **Secondary Prevention:** Low-dose aspirin (Ascard, Loprin) at dose 75mg, starting at 12–14 weeks' gestation) is recommended in subsequent pregnancies. If the risk of preeclampsia is thought to be high (e.g., previous early-onset disease, severe disease), the benefits are clear. However, they are less clear in mild to moderate or late disease, where the outcome is typically good anyway.

» **Corticosteroids for fetal lung maturity: Indications** - anticipated delivery between 24 and 34 weeks' gestation

- » Inj. Betamethasone 4mg/1ml (Betnesol) x 12mg x IM x once daily for 2 days
- OR Inj. Dexamethasone 4mg/1ml (Decadron) x 6mg x IM x twice daily for 2 days.



ECLAMPSIA

- ☞ **Onset:** The majority of cases occur intrapartum and postpartum.
- ☞ **Eclampsia** is a New-onset seizures, superimposed upon preeclampsia, in any pregnant woman who is at ≥ 20 weeks of gestation or < 4 weeks postpartum who develops seizures, coma, or encephalopathy. Occasionally, eclampsia can present with seizure in the absence of blood pressure elevation and proteinuria.
- ☞ Most often associated with severe preeclampsia
- ☞ **Eclamptic seizures:** Generalized tonic-clonic seizures (usually self-limited)

TREATMENT OF ECLAMPSIA

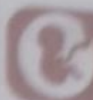


- ☞ Admit (Hospitalized) the patient
- ☞ Initiate ABCD&E approach with measures taken to avoid aspiration.
- ☞ Administer supplemental oxygenation as appropriate
- ☞ Position patient on left lateral decubitus position to prevent placental hypoperfusion through compression of the inferior vena cava and reduce the risk of aspiration in the mother.
- ☞ Start Anticonvulsive therapy to control seizures:
 - » **First-line: Inj. Magnesium sulfate 500mg/1ml** (Zafa Pharma) at loading dose of 4–6 g IV in 100ml to 150ml 0.9% NS administered over 15 to 20 minutes. (A second loading dose of 2–4 g IV may be given for patients experiencing eclamptic seizures) followed by 1–2 g/hour IV infusion (25 ml/hour to 50 ml/hour).
 - **Magnesium sulfate (Mg So₄)** is contraindicated in patients with myasthenia gravis and should be administered with care in patients with renal insufficiency.
 - **Monitoring for magnesium toxicity (hypermagnesemia) for at least every 1-2 hours.**
 - ☞ Monitor all patient for clinical signs of magnesium toxicity → deep tendon (patellar) reflexes ↓, BP ↓, respiratory rate ↓ (respiratory depression), poor urine output (oliguria), slurred speech, Diaphoresis → stop magnesium and check serum magnesium levels
 - ☞ Administer Inj. Calcium gluconate 10%/10ml (1g/10ml) x IV over 3 minutes and consider diuretics (e.g., IV furosemide, IV mannitol).
 - » **Seizures unresponsive to magnesium sulfate**
 - ☞ Amobarbital or phenytoin
 - ☞ Consider intubation and assisted ventilation and give general anesthesia.
 - ☞ Managing the airway in pregnancy can be challenging; consult anesthesia early.
 - ☞ **Persistent postictal low GCS scores or focal neurological signs:** Consult neurology.
- ☞ Start antihypertensives for urgent blood pressure control in pregnancy.
- ☞ **Expectant management** in patients < 34 weeks' gestation to allow time for corticosteroid administration can be considered in select cases, but the safety and benefits of this approach have not been confirmed
 - » Start continuous fetal monitoring.
 - » Eclampsia is an indication for immediate delivery regardless of gestational age.
 - » **Delivery:** once the mother is stable and seizures have stopped.
 - » Eclampsia is not an indication for cesarean delivery.

ACUTE FULMINANT PRE-ECLAMPSIA

- ☞ **Acute fulminant pre-eclampsia (Pre-eclamptic State)** is a clinical entity where the onset of the pre-eclamptic manifestations is acute, occurring de novo or there is rapid deterioration in an established case of pre-eclampsia with severe hypertension over a short period of time. There is a constant threat of seizures, cerebral hemorrhage, heart failure or placental abruption. All the features of severe preeclampsia are intensified.
- ☞ If seizures/fits detected at home, or at a primary health care facility/clinic, the patient should be adequately sedated by administration Inj. Midazolam 5mg/5ml (Dormicum) 1–2 mg/kg/dose, IV STAT, may be repeated in 5–10 minutes OR Inj. Diazepam 10mg/2ml (Valium) x diluted in 8ml 0.9% NS x IV slow.
- ☞ **Prophylactic magnesium sulphate** should be given when possible. She should be shifted as gently as possible with an attendant doctor or a midwife, to tackle the fit/seizure, if it occurs during the journey to the hospital.

EPILEPSY IN PREGNANCY



DIAGNOSTIC APPROACH

Diagnosing epilepsy in pregnant women follows the same general principles as in non-pregnant women, but with added considerations to ensure both maternal and fetal safety.

- **History and Physical Examination:** Detailed history taking is crucial, focusing on seizure type, frequency, triggers, and current medication regimen. Physical examination helps rule out other causes of seizures.
- **Electroencephalogram (EEG):** An EEG is essential to confirm the diagnosis and classify the type of epilepsy, guiding treatment of epilepsy.
- **MRI** is preferred over CT scans due to the absence of ionizing radiation, making it safer for the fetus.
- **Blood Tests:** These include baseline measurements of anti-epileptic drug (AED) levels, complete blood count, liver and kidney function tests, and metabolic panel.

MANAGEMENT GUIDELINES OF EPILEPSY

Managing epilepsy in pregnant women aims to control seizures while minimizing risks to the fetus from both the seizures and the medication.

1. **Preconception Counseling:** Women with epilepsy should receive counseling before conception. This includes discussing the risks of teratogenicity from AEDs, the importance of seizure control, and folic acid supplementation (5 mg/day) to reduce the risk of neural tube defects.
2. **Medication Management:**
 - **Monotherapy:** Whenever possible, monotherapy with the lowest effective dose is preferred to reduce teratogenic risks.
 - **Drug Choices:** Some AEDs are safer during pregnancy. Lamotrigine and levetiracetam are considered relatively safer options. Valproate, phenytoin, and phenobarbital are associated with higher risks of congenital malformations and should be avoided if possible.
 - **Dose Adjustments:** Pregnancy can alter drug metabolism, requiring dose adjustments. Regular monitoring of drug levels is crucial to maintain therapeutic levels.
 - **Vitamin K:** Vitamin-K supplementation (10 mg/day orally during the last month of pregnancy) is recommended to prevent neonatal hemorrhage, especially in women taking enzyme-inducing AEDs.
3. **Seizure Management:**
 - **General Precautions:** Pregnant women with epilepsy should avoid known seizure triggers, ensure regular sleep patterns, and maintain good medication adherence.
 - **Acute Seizure Management:** In case of a seizure, immediate medical evaluation is necessary. Intravenous benzodiazepines (like lorazepam, Diazepam) can be used for acute seizure control.
4. **Folic Acid Supplementation:** High-dose folic acid (5 mg/day) is recommended preconceptionally and during pregnancy to reduce the risk of neural tube defects, which are more common in women taking AEDs.
5. **Monitoring and Follow-up:**
 - **Regular Prenatal Visits:** More frequent prenatal visits are necessary to monitor both maternal and fetal well-being.
 - **Ultrasound Scans:** Detailed anomaly scans are recommended, typically at 18-20 weeks, to detect structural abnormalities.
 - **Non-stress tests & Biophysical profiles:** These may be used in the 3rd trimester to monitor fetal well-being.
6. **Delivery and Postpartum Care:**
 - **Delivery Plan:** Delivery should be planned in a hospital with facilities for neonatal and maternal intensive care if needed. Vaginal delivery is preferred unless there are obstetric indications for cesarean section.
 - **Postpartum Care:** Monitoring AED levels postpartum is important as drug metabolism changes back to pre-pregnant states. Breastfeeding is generally encouraged, but the choice of AEDs may need to be considered to minimize exposure to the infant.



MIGRAINE HEADACHE IN PREGNANCY

- Treatment of migraine in pregnancy are same as non-pregnant patients – see migraine neurology section.
- Most patients see an improvement in migraine frequency as the pregnancy progresses; therefore, address red flag symptoms and consider other life-threatening causes of severe headache (central venous thrombosis) especially in the 2nd or 3rd trimester before diagnosing migraine. Although the ergot alkaloids are **CONTRAINDICATED IN PREGNANCY**, Triptans: Sumatriptans (class C) do not appear to increase fetal malformations, and if already prescribed by the OB/GYN or primary physician during pregnancy, sumatriptans can be continued as an outpatient



TREATMENT OF MIGRAINE HEADACHE IN PREGNANCY

1. Pain control
 - » First-line: Tab. Paracetamol 500mg (Calpol, Panadol) OR Tab. Paracetamol 500mg + Caffein (Panadol Extra, Calpol plus) x at dose 500mg to 1000mg x TDS
 - » Second-line: NSAIDs (safe to use until the end of the 2nd trimester of pregnancy)
Tab. Naproxen sodium 250mg OR Tab. Diclofenac sodium 50mg OR Tab. Ibuprofen 400mg x TDS
 - » Third-line
 - ↳ Triptans: can potentially cause constriction of uterine vessels and uterine contractions
 - ↳ Opioids: can cause neonatal withdrawal syndrome and exacerbate nausea/vomiting
 - » Ergot derivatives (Migril) are contraindicated because they induce uterine contractions.
2. Control of nausea/vomiting: the following medications are safe to use in pregnancy
 - » Tab. Metoclopramide 10mg (Maxolon, Metoclon) x 1 – 1 – 1 (TDS)
 - » OR Tab. Diphenhydramine 25mg (Benadryl) x 1 – 1 – 1 (TDS)
 - » OR Tab. Prochlorperazine 5mg (Stemetil) x 1 – 1 – 1 (TDS)
 - » OR Tab. Promethazine 25mg (Phenergan) x 1 – 1 – 1 (TDS)
 - » OR Tab. Ondansetron 4mg (Onset, Onseron) x 1 – 1 – 1 (TDS)
3. Prophylactic therapy
 - » First-line: Beta-blockers (Propranolol, Cyproheptadine), Calcium channel blockers
 - » Second-line: SSRIs and SNRIs (except paroxetine), Gabapentin

MENSTRUAL MIGRAINE

- **Definition:** It is characterized by an attack of migraine that occurs either perimenstrually or both perimenstrually and also at other times. Treatment includes drugs of migraine (triptans)/or others (NSAIDs).



TREATMENT OF MENSTRUAL MIGRAINE

(For further treatment and prevention – see migraine neurology section)

- **Lifestyle Modifications:**
 - » Regular exercise: Helps in maintaining overall health and reducing stress.
 - » Healthy diet: Avoiding known dietary triggers and maintaining a balanced diet.
 - » Hydration: Ensuring adequate fluid intake.
 - » Sleep hygiene: Regular sleep patterns can help reduce migraine frequency.
- NSAIDs: Tab. Naproxen sodium 250mg (Flexin, Neoprox) at dose 500mg once, followed by 250mg three times daily OR Tab. Mefenamic acid 500mg (Ponstan forte, Dollar DS, Mefnac DS) x two or three times daily, 48 hours before expected attack for 4 to 10 days.
- Triptans, if not respond, starting 2 days before the expected onset of menstruation and continue as required
 - » Sumatriptan: 50-100 mg at onset. A second dose (up to 100 mg) may be taken after 2 hours if needed. Maximum daily dose: 200 mg.
 - » Zolmitriptan: 2.5-5mg at onset. A second dose may be taken after 2 hours if needed. Max daily dose: 10mg
- Gastroprotective: Cap. Esomeprazole 40mg (Esso, Eskem) x once daily

GASTROESOPHAGEAL REFLUX DISEASE (GERD) IN PREGNANCY

- **Definition:** Gastroesophageal reflux disease (GERD) is extremely common in pregnancy. GERD is characterized by epigastric pain or burning radiating into the chest and neck, pain with recumbency, and pain exacerbated by acidic foods. Symptoms increase in the second trimester and peak in the third trimester due to loosening of the lower esophageal sphincter and delayed gastric emptying from pregnancy-related hormones.
- Endoscopy is considered if therapeutic measures are unsuccessful, and symptoms are very severe.

TREATMENT OF GERD IN PREGNANCY

- **Lifestyle changes:** Always reinforce lifestyle modifications
 - » Elevating the head of the bed at night
 - » Not eating 3 hours before bedtime
 - » Eating light meals, Eliminating trigger foods.
 - » Dietary modification is recommended, including reduced consumption of fatty foods, chocolate & caffeine.
 - » Cigarette smoking and alcohol consumption can exacerbate GERD and are discouraged in all patients.
 - » **Hydration:** Drink plenty of water throughout the day but avoid large amounts with meals to prevent distension of the stomach.
 - » **Ginger:** Can be helpful for nausea and may have some benefit for GERD. Ginger tea or ginger supplements can be taken in moderation.
 - » **Monitor Weight Gain:** Excessive weight gain can increase abdominal pressure and worsen GERD symptoms.
- **Medical treatment**
 - » **Tab. Famotidine 40mg** (Famot, Acicon, Famobex) x 1 – 0 – 1 (BD)
 - OR **Cap. Esomeprazole 20mg** (Eskem, Esso, Esante) x 1 – 0 – 1 (BD) x کھاتے سے 30 منٹ پہلے
 - OR **Tab. Pantoprazole 20mg** (Zopent, Neege, Protium) x 1 – 0 – 1 (BD) x کھاتے سے 30 منٹ پہلے
 - » **Syp. Aluminium + Magnesium hydroxide** (Mylanta-2, Manacid, Mucaïn, Maalox) x 2 teaspoonful x BD
 - » **Other agent:** Syp/Tab. Sucralfate 1g x TDS, Tab. Metoclopramide

PEPTIC ULCER DISEASE IN PREGNANCY

△ Peptic ulcer disease (PUD) c/c:

- PUD is not common in pregnancy, and the hormonal changes of pregnancy usually decrease PUD severity and symptoms.
- Treatment during pregnancy is similar to treatment for GERD and consists of diet modification
- Avoiding nonsteroidal anti-inflammatory drugs (NSAIDs) and starting H2 blockers or proton pump inhibitors. Avoid indomethacin for tocolysis of patients with PUD.



1. Lifestyle and Dietary Modifications

- » Eat small, frequent meals.
- » Avoid spicy, fatty, and acidic foods.
- » Avoid caffeine and carbonated beverages.
- » Avoid alcohol and smoking.
- » **Stress Management:** Practice relaxation techniques such as yoga, meditation, and deep breathing exercises.
- » **Elevate Head of Bed:** To reduce nighttime symptoms, elevate the head of the bed.

2. **Tab. Famotidine 20mg or 40mg** (Famot, Acicon, Famobex)
1 – 0 – 1 (20mg = BD) 'OR' 0 – 0 – 1 (40mg = OD)
OR **Cap. Esomeprazole 20mg or 40mg** (Eskem, Esso, Esante)
OR **Tab. Pantoprazole 20mg or 40mg** (Zopent, Neege, Protium)
1 – 0 – 1 (20mg = BD) 'OR' 0 – 0 – 1 (40mg = OD)
کھاتے سے 30 منٹ پہلے
(Mylanta-2, Manacid, Mucaïn, Maalox)

3. **Syp. Aluminium + Magnesium hydroxide**
2 teaspoonful x BD



HELICOBACTER PYLORI IN PREGNANCY

Clinical features and diagnosis same as non-pregnant – See GIT section

Tetracycline: Not recommended during pregnancy due to potential risks to the fetus (FDA category D).

General considerations

- » **Timing:** If the infection is not causing severe symptoms or complications, some providers may recommend delaying treatment until after the first trimester or even until after delivery, depending on the patient's condition.
- » **Risk vs. Benefit:** The decision to treat should be based on the balance of potential benefits and risks to the mother and fetus.



H. PYLORI MODIFIED REGIMEN

1. Diet and Nutrition

- » **Avoid Trigger Foods:** Some foods can aggravate stomach irritation and should be avoided. These include Spicy foods, Fatty and fried foods, Acidic foods (such as citrus fruits and tomatoes), Caffeinated beverages (coffee, tea, soda), Alcohol
- » **Eat Smaller, Frequent Meals:** Eating smaller, more frequent meals can help reduce stomach acid production and alleviate symptoms.
- » **Stay Hydrated:** Drink plenty of water throughout the day to help maintain good digestion.

2. Tab. Amoxicillin 1g (Zeemox, Ospomox)

1-0-1 (1 tablet twice daily)

OR Cap. Amoxicillin 500mg (Amoxil, Zeemox, Ospomox)

2-0-2 (2 capsule x Twice daily)

OR Tab. Metronidazole 400mg (Klint, Flagyl)

1-1-1 (TDS) – Generally avoided in the first trimester but may be used in the 2nd and 3rd trimesters if necessary (FDA category B).

3. Tab. Clarithromycin 500mg (Claritek, Klaricid, Ultima)

1-0-1 (BD) – Usually avoided in the first trimester but may be used in the 2nd and 3rd trimesters if necessary (FDA category C).

4. Cap. Esomeprazole 20mg (Nexum, Esso, Esante)

OR Tab. Pantoprazole 20mg (Zopent, Neege, Protium)

1-0-1 (BD) کھانے سے 30 منٹ پہلے

CONSTIPATION IN PREGNANCY

Clinical features

- » Abdominal pain or discomfort
- » Difficult and infrequent bowel movements
- » The passage of hard stools.

Constipation in pregnancy is common complaint due to

1. High hormonal level especially of progesterone which slow down the intestinal rhythm.
2. Increased pressure of growing fetus on intestinal loops.
3. Less water due to less fluid intake and emesis.
4. Side-effects of iron supplementation



- » **Drink a lot of fluids:** Drink 10 to 12 cups of fluids each day.
- » **Exercise routinely:** Schedule exercise three times a week for 20-30 minutes each.
- » **Eat a high fiber diet:** Choose high-fiber foods, such as fruits, vegetables, beans and whole grains.
- » **Reduce or eliminate iron supplements**
- » **Natural Remedies**
 - » **Prune Juice:** Prune juice is a natural laxative. Drink 4-6 ounces once or twice daily.
 - » **Warm Liquids:** Drinking warm liquids, especially in the morning, can help stimulate bowel movements.
- 1. **Psyllium fiber supplement powder** (Fibrocol, Metamucil, Fibo) 1-tablespoon mixed with water, 1-3 times daily.
- 2. **Syp. Lactulose** (Duphalac, Lilac) x 15-30 ml once or twice daily. Lactulose is a synthetic sugar used to treat constipation by drawing water into the bowel.

IRON DEFICIENCY ANEMIA (IDA) IN PREGNANCY



Clinical features

Nonspecific and related to both severity and the cause of the anemia (e.g. gastrointestinal disease)

- » Onset: Insidious.
- » Nonspecific symptoms:
 - » Chest pain and dyspnea on exertion
 - » Fatigue, palpitations, breathlessness, weakness and irritability.
 - » Pharyngeal/esophageal webs formed cause dysphagia.
- » Patterson-Kelly or Plummer-Vinson syndrome:
 - » Microcytic hypochromic anemia
 - » Atrophic glossitis
 - » Esophageal webs
- » Congestive heart failure in severe anemia.
- » Pica (craving for non-nutritive substances, such as ice, dirt, or starch)
- » Physical Findings: Diminished tissue enzymes cause characteristic epithelial changes of iron deficiency anemia.
 - » Angular stomatitis and glossitis
 - » Chronic atrophic gastritis
 - » Koilonychia (spoon nails).

Treatment Guidelines

- » 180-200mg iron supplement is given TWICE DAILY till blood parameters become normal, followed by ONCE DAILY as maintenance dose should be continued throughout pregnancy and for 3 months after replenishing the stores.
- » WHO recommendations are 6 months in countries with a prevalence anaemia <40% and for additional 3 months post-partum (prevalence >40%)

Diagnostic workup

- » CBC: ↓ hb (<11 g/dL), ↓ MCV (<76 femtoliters), ↓ MCH & MCHC
- » Peripheral blood smear: Shows microcytic (small) and hypochromic (pale) red blood cells.
- » Serum iron profile (Iron studies)
 - » Reduced: Serum iron, Ferritin, % transferrin receptor saturation.
 - » Increased: TIBC, TFR and Red Cell Protoporphyrin.



Treatment of Iron deficiency anemia in pregnancy

1. Dietary Modifications:
 - » Increase intake of iron-rich foods: red meat, poultry, fish, lentils, beans, leafy green vegetables, fortified cereals, and nuts.
 - » Enhance iron absorption by consuming vitamin C-rich foods (e.g., citrus fruits, tomatoes) alongside iron-rich foods.
2. Oral iron supplementation:
 - » Tab. Ferrous sulphate 150mg + Folic acid + B-Complex (Fefol, FefolVit, Fervit)
 - » OR Tab. Elemental Iron 105mg + Folic acid 800mcg + B-Complex (Iberet-Folic)
 - » OR Tab. Iron Polymaltose 100mg + Folic Acid 0.35mg (Maltofer-Fol, Ferosoft-FA, Malcifer-F, Polymalt-F) 0-0-1 (OD) OR 1-0-1 x (BD) x orally once or twice daily.
 - » OR Syp. Iron Polymaltose 100mg + Folic Acid 0.35mg (Maltofer-Fol, Ferosoft-FA, Malcifer-F, Polymalt-F) 2-0-2 (2 Teaspoonful x BD)
3. Adjunct: Tab. Vitamin-C 500mg (Tab. Cecon) x once daily
 Instructions: Take iron supplements on an empty stomach or with a source of vitamin C to enhance absorption. Avoid taking with calcium-rich foods, antacids, or calcium supplements, as they can inhibit iron absorption.
4. Treatment of hook worm infection: by single dose of Albendazole 400mg or Mebendazole 100mg twice daily for 3 days to all anaemic pregnant women before pregnancy or after the 1st trimester of pregnancy.
5. Intravenous (IV) iron therapy: Indicated when oral iron is not tolerated, not effective, or when rapid replenishment of iron stores is needed. (See haematology section)
 - » Iron Sucrose: 200 mg IV over 2-5 minutes or diluted in 100 mL of normal saline and infused over 15-30 minutes.
 - » Ferric Carboxymaltose: 750-1000 mg IV in a single dose, repeated after one week if necessary.



MEGALOBlastic ANEMIA (FOLIC ACID & VITAMIN-B12) IN PREGNANCY

CLINICAL FEATURES OF MEGALOBlastic ANEMIA (MBA)

1. Clinical features of Folic Acid deficiency anemia
 - ☞ Onset: insidious and progresses slowly.
 - ☞ Signs of anemia: fatigue, pallor palpitation, dyspnea on exertion
 - ☞ Mild scleral icterus and/or jaundice
 - ☞ ± Splenomegaly
2. Clinical features of Vitamin-B12 Deficiency anemia:
 - ☞ Clinical features of Folic acid deficiency anemia **"PLUS"**
 - ☞ Neurological disturbances are generally symmetrical
 - » **Peripheral neuropathy:** tingling, numbness, pins-and-needles sensation, coldness (especially in the lower extremities)
 - » **Subacute combined degeneration of spinal cord:** symmetrical demyelination of the spinal cord tracts occurs in vitamin B12 deficiency due to insufficient vitamin B12-dependent fatty acid synthesis and production/maintenance of myelin.
Subacute combined degeneration of spinal cord may be manifests with the following symptoms:
 1. Paresthesia, impaired proprioception, loss of vibratory sensation, tactile sensation, and position discrimination due to demyelination of the dorsal columns
 2. Spastic paresis due to demyelination of the lateral corticospinal tracts (axons of UMN)
 3. Gait abnormalities (spinal ataxia) resulting from the damage of spinocerebellar tracts and dorsal columns
 - » **Neuropsychiatric disease:** Reversible dementia, depression, paranoia

Diagnostic workup

Note: Blood findings in vitamin B12 and/or folic acid deficiency are similar

- ☞ **CBC:** ↓ hb (<11 g/dL), ↑ MCV (>96 femtoliters), ↓ WBC count (leukopenia), ↓ Platelets
- ☞ **Peripheral blood smear:**
 - **Pancytopenia:** Decreased RBC, WBCs and platelets
 - Macrocytic and oval (egg-shaped **macro-ovalocytes**) - **Diagnostic.**
 - **Hypersegmented neutrophils** (more than five nuclear lobes) - **Hallmark feature**
The first and most specific morphological sign of megaloblastic anemia

☞ Investigation of choice

1. Decreased Serum **folic acid level** – folic acid deficiency anemia
2. Decreased Serum **vitamin B12 level** – vitamin B12 deficiency anemia
Normal value of vitamin B12: >240 pg/ml, **Borderline level:** 170-240 pg/ml
Vitamin B12 deficiency: <170 pg/ml (For further test see MBA hematology section)



TREATMENT OF MEGALOBlastic ANEMIA

- ☞ **Dietary sources**
 - » **Folic acid:** Leafy green vegetables, citrus fruits, beans, and fortified cereals.
 - » **Vitamin B-12:** Meat, poultry, fish, dairy products, eggs, and fortified cereals. For vegetarians/vegans, B12-fortified foods or supplements are essential.
- ☞ **Inj. Methylcobalamin 500mcg** (Methylcobal, Neuromet, Cobalamin) x 2 ampule (=1000mcg = 1mg) x IM, in 5 doses at 2-3 days apart (a total of 5 mg), followed by maintenance therapy of 1000 mcg (1mg) every 3 months for the rest of the life.
- ☞ **Tab. Methylcobalamin 500mcg** (Methylcobal, Cobalamin, Neuromet) x BD
- ☞ **Tab. Folic acid 5mg** x OD for 3 weeks cures acute deficiency, while 5mg once weekly is for maintenance dose



GESTATIONAL DIABETES MELLITUS (GDM)

Definition: Historically, GDM has been defined as the diagnosis of clinically significant impaired glucose tolerance in pregnancy in a woman not previously known to be diabetic. This has recently been complicated by recognizing that some diabetes mellitus will present for the first time in pregnancy and lack of clarity as to where the lower threshold for diagnosis should best be placed.

△ GDM
C/C:

For diagnosis see DM
Endocrine section

Clinical consequences of
gestational diabetes mellitus

Maternal

- » Pre-eclampsia
 - » Caesarean section
- Fetal
- » Birth weight greater than the 90th percentile
 - » Preterm birth (<37 weeks)
 - » Shoulder dystocia and/or birth injury
 - » Neonatal hypoglycaemia
 - » Neonatal hyperbilirubinaemia
 - » Neonatal intensive care unit admission
 - » Placental insufficiency
 - » Perinatal mortality

Rx

TREATMENT OF GDM

Management for Gestational Diabetes Mellitus (GDM) initially consists of diet and exercise. If good glucose control is not achieved, less than 20% of women requiring oral hypoglycemic agents (Metformin) or insulin.

- » Women with newly diagnosed Gestational Diabetes Mellitus (GDM) are started on a diabetic diet of 1,800 to 2,400 kcal/day
- » Regular exercise also is important in the control of blood sugar but should be limited to mild to moderate levels of exertion only. A common recommendation is a 30-minute walk during the day or after the evening meal
- » Patients are encouraged to maintain a consistent level of activity throughout pregnancy provided there are no complications (e.g., preterm labor).
- » **Insulin therapy can improve glycemic control for GDM.** Different types of insulin are combined to maintain even control through day and night
- » **Neutral Protamine Hagedorn (NPH) insulin** is an intermediate-acting insulin given in the **morning** and at **night**, with peak activity at 5 to 12 hour.
- » **Rapid-acting insulin** (Humalog or Novolog) is administered with meals because its onset is 5 to 15 minutes and peak activity occurs at 2 to 4 hour.
- » **Fetal monitoring** is not required for GDM-A1 diabetics. They are not at increased risk for fetal demise before 40 weeks' gestation. Women with GDM-A2 (i.e., on medication) require antenatal testing similar to that recommended for pregestational DM (twice weekly NSTs or BPP from 32 to 34 weeks until delivery). Delivery by 40 weeks' gestation is recommended.

Total Initial Insulin Dose
(usually not more than 60 units/day to start)
0.7 units/kg at 6-18 weeks
0.8 units/kg at 18-26 weeks
0.9 – 1.1 units/kg at >26 weeks

1/2 of the total dose
in the morning

1/2 of the total dose
in the evening

2/3 as NPH at
breakfast

1/3 as rapid acting
insulin at breakfast
(Humalog or Novolog)

1/2 as NPH at
bedtime

1/2 as rapid acting
insulin at dinner
(Humalog or Novolog)

Calculation and dose distribution for initial insulin management in pregnancy. (Adapted from Gabbe SG. Management of diabetes mellitus complicating pregnancy. *Obstet Gynecol* 2003;102(4):857.)

Complications to Watch For

- » **Maternal Complications:** High blood pressure, preeclampsia, increased risk of cesarean delivery.
- » **Fetal Complications:** Macrosomia (large baby), hypoglycemia (low blood sugar) after birth, jaundice, and increased risk of developing obesity or type 2 diabetes later in life.



HYPOGLYCEMIA IN PREGNANCY

Clinical features	Rx
- Shakiness - Sweating - Dizziness - Paresthesia - Hunger - Irritability - Confusion - Palpitations - Anxiety - Palpitations Severe cases: - Loss of consciousness - seizures	Education and Planning: - Educate the patient and family members about recognizing and treating hypoglycemia. - Carry glucose tablets or other sources of fast-acting carbohydrates at all times. Immediate Treatment for Hypoglycemia Consume Fast-Acting Carbohydrates: 15-20 grams of glucose or simple carbohydrates: Examples include glucose tablets, half a cup (4 ounces) of juice or regular soda, 1 tablespoon of honey or sugar, or hard candies. Recheck Blood Sugar: Check blood sugar 15 minutes after treatment. If it's still below 70 mg/dL (3.9 mmol/L), repeat the above steps. Follow-Up with a Meal or Snack: Once blood sugar levels are back to normal, eat a meal or snack that contains protein and carbohydrates to stabilize levels. - If the patient is unable to tolerate food and drink than provide standard treatment for severe hypoglycemia, with an ampule of IV dextrose 10% or PO glucose or glucagon 1 to 2 mg SC, IM, or IV, followed by IV fluids containing 5% dextrose.
Diagnosis	
- Careful history & review of symptoms Blood Glucose Monitoring: Checking blood sugar levels with a glucometer during symptoms can confirm hypoglycemia (typically <70 mg/dL or <3.9 mmol/L).	

SOMOGYI EFFECT

- The Somogyi effect is rebound hyperglycemia after hypoglycemia, secondary to counterregulatory hormone release.
- It usually occurs in the middle of the night but can happen after any hypoglycemic episode, manifesting as wide variations in blood glucose levels over a short period of time (e.g., between 2:00 and 6:00 a.m.).
- Diagnosis is by checking additional blood sugars (i.e., 3:00 a.m.) to identify unrecognized hypoglycemia.
- Treatment involves adding or modifying a nighttime snack or decreasing the overnight insulin dose in order to better match insulin needs with dietary intake.

DAWN PHENOMENON

- The dawn phenomenon is also an early morning increase in plasma glucose, possibly due to normal nighttime production of growth hormone (GH), catecholamines, and cortisol.
- It is also diagnosed by checking early morning (i.e., 3:00 a.m.) blood sugar level.
- If the patient is euglycemic overnight, she may require increased bedtime insulin dosing to cover the effect of normal morning hormones.
- Differentiating between the Somogyi effect and the dawn phenomenon helps tailor the insulin regimen and achieve optimal glucose control.

**DIABETIC KETOACIDOSIS (DKA) IN PREGNANCY**

DKA is a serious medical and obstetrical emergency previously considered typical of type 1 diabetes but now reported also in type 2 and gestational diabetes patients. The incidence of DKA in pregnancy decreases with early diagnosis of insulin-dependent diabetes, improved prenatal counseling, and care with an identifiable primary care provider. DKA still most commonly affects women in the 2nd or 3rd trimester or pregnant women with new-onset type 1 diabetes. A pregnant diabetic who is ill appearing, has persistent nausea and vomiting, and/or has a blood glucose level ≥ 180 mg/dL [9.99 mmol/L] should be screened for DKA with serum or urine ketones and a serum chemistry panel. Diabetic pregnant women at > 20 weeks of gestation are more prone to develop more severe and rapidly progressive episodes of DKA (usually over hrs.) and at lower glycemic levels (< 300 mg/dL [< 16.65 mmol/L]).

Management guidelines for pregnant women with DKA are the same as for non-pregnant patients. In addition to the usual care, obtain fetal heart tones, administer oxygen, and for third-trimester patients, place patient in the left lateral decubitus position to displace the uterus and improve uterine blood flow. Most fetal heart rate abnormalities subside after correction of maternal hypovolemia and acidosis. DKA is not an indication for delivery. Although fetal heart rate monitoring in maternal DKA may initially demonstrate a non-reassuring pattern, patterns usually improve as maternal ketoacidosis is corrected, and mother will tolerate delivery or cesarean section better once acidosis resolves.

TREATMENT OF DIABETIC KETOACIDOSIS (DKA) IN PREGNANCY

For more detail (Diagnosis & Clinical features) → see DKA (Endocrine section)

1. **Airway:** Ensure patient is maintaining own airway, sit patient up to prevent acidosis
2. **Breathing:** Check SpO_2 and correct hypoxia with supplementary O_2 , watch for Kussmaul breathing, which may be present to compensate for metabolic acidosis.
3. **Circulation:**
 - » **Vitals Monitor:** BP, PR, RR, Temperature, SpO_2 x 4 hourly
 - » **Maintain 2 large bore intravenous line x (20 gauge)**
 - » **Monitor labs:** Blood sugar level x 1 hourly, ABGs x 4 hourly, Input/output record x 1-4 hourly, electrolytes 4 hourly
 - » **Insulin therapy: Pak.*Brands (Humulin-R/Actrapid/Insuget-R)**
 1. Inj Regular Insulin x 5-10 units x IV (0.14 mg/kg) + 5-10 units x Subcutaneous (0.4 mg/kg) x stat
 2. **Insulin Infusion:** 60 units of Regular insulin injection with 100ml 0.9% N/S is prepared in 100ml IV chamber x IV x 10 mic drops/minute start if $K^{++} > 3.5$
 3. Not to start IV Insulin if K^{++} level is < 3.3 , Maintain serum potassium between 4-5 mEq/L.
 4. Continuous IV insulin infusion until the anion gap is normal
 5. Once anion Gap is normal then shift the Patient to S/C (Subcutaneous) insulin
 - » **Fluid replacement therapy:** Extracellular fluid loss is replaced by 0.9% N/S (isotonic solution), Intracellular fluid loss is replaced by Dextrose 5% or 10%. **(Fluid of choice is 0.9% N/S or 0.45% N/S)**
 - » **First hour:** 0.9% N/S 1000ML to 1500ML (or 1-2L) bolus fluid at 15-20 mL/kg/hour
 - » **Next 24-48 hours:** Adjust Intravenous fluid rate and composition according to CVP, urine output, blood glucose, and corrected sodium levels.
 - » **Add 20ml (20-40mEq/L) of KCL to each Liter of 0.9% of N/S once K^{++} is < 5.5**
 - » Than 1L of 0.9% N/S in 2 hours
 - » Than 1L of 0.9% N/S in 4 hours
 - » Than 1L of 0.9% N/S in 6 hours
 - » Than 1L of 0.9% N/S in 8 hours.
 - » Start 5% Dextrose if RBS value is $< 200-250$ mg/dL at the rate 125ml IV/hour
 - » If RBS value is > 250 mg/dL changed dextrose into 0.9% N/S
4. **Disability & Exposure (Secondary Survey)**
 - » Consider early HDU/ICU Admission
 - » NPO status in patients with high anion gap metabolic acidosis on insulin infusion
 - » Pass Nasogastric tube and foley's catheter
 - » Monitor pupillary reflexes and GCS level



HYPERTHYROIDISM/THYROTOXICOSIS IN PREGNANCY

- ☛ **Definition:** Hypothyroidism in pregnancy is rare, affects 1 in 800 pregnancies (< 0.5% of cases). The majority of cases have Graves' disease. Rarer causes of hyperthyroidism in pregnancy are toxic nodule, thyroid adenoma, carcinoma, or subacute thyroiditis. Many clinical features of hyperthyroidism also occur in normal pregnancy, for example, palpitations, heat intolerance, and palmar erythema. However, eye signs and pretibial myxoedema are specific to autoimmune thyroid disease and weight loss does not occur in normal pregnancy.
- ☛ **Etiology:** Graves' disease and β -hCG-mediated hyperthyroidism are the most common causes.
- ☛ **Pathogenesis**
 - » β -hCG molecule has a similar structure to that of the TSH molecule.
 - » β -hCG binds to TSH receptors of the thyroid gland $\rightarrow$ thyroid stimulation $\rightarrow$ hyperthyroidism
- ☛ Presentation may be asymptomatic or include disproportionate weight gain, lethargy, weakness, constipation, carpal tunnel syndrome, cold sensitivity, hair loss, dry skin, and eventually myxedema.
- ☛ **Diagnostic workup** same as in nonpregnant patients, but nuclear medicine thyroid scan is contraindicated.
- ☛ **Complications:** if left untreated $\rightarrow$ miscarriage, stillbirth, preeclampsia, premature labor, cardiac failure, low birth weight, neonatal hyperthyroidism



TREATMENT OF HYPERTHYROIDISM/THYROTOXICOSIS IN PREGNANCY

- ☛ **Treatment of hyperadrenergic symptoms:** Beta-blockers (first-line) are used for symptom management in thyrotoxicosis until thyroid hormone levels are normalized with suppressive therapy. Adverse side effects include decreased ventricular function resulting in pulmonary edema.
 - » Tab. Propranolol 10mg OR 40mg (Inderol, Cardinol) at dose 10 to 40mg per orally every 4 to 6 hour to maintain heart rate below 100 bpm.
- ☛ **Antithyroid drugs:**
 - » **First trimester:** Tab. Propylthiouracil 50mg (Procarbazole, PTU) 50–150 mg PO every 8–12 hours (100–450mcg/day in two divided doses); titrate as needed and continued till the patient becomes euthyroid. Measurement of serum TSH & Free-T4 should be checked every 2 to 4 weeks until on stable medication dosage. Maximum of 1,200mg daily to maintain.
 - » **2nd and 3rd trimester:** carbimazole is the most sensible choice after the first trimester.
 - ↳ Tab. Carbimazole 5mg (Neomarcazole) at dose 10 to 40mg orally every 12 hours; titrate as needed and maintained at this dose until the patient becomes euthyroid. Then it is progressively reduced to a maintenance of between 5 and 15 mg daily.
- » **Monitoring**
 - ↳ Obtain baseline test prior to therapy: CBC, LFTs, Repeat if febrile illness or symptoms of liver injury.
 - ↳ TFTs: measure free T4 and T3, 2–6 weeks after initiation of therapy and adjust dosage accordingly.
- » **Duration of therapy:**
 - ↳ Primary therapy for Graves' disease is typically 12–18 months
 - ↳ Preparation for surgery: given until TFTs normalize, after which surgery may be performed
- » **Treatment goal:** Serum Free thyroxin (Free T4) level in upper one-third of normal range.
- ☛ **Methimazole and propylthiouracil (PTU) are equally efficacious in the treatment of pregnant women.** However, both medications have potential adverse effects. Methimazole is associated with congenital abnormalities during first-trimester organogenesis and has been linked to esophageal and choanal atresia and aplasia cutis. Propylthiouracil can cause hepatotoxicity. Recent studies revealed that children exposed to propylthiouracil also developed birth defects. Therefore, current recommendations are to confirm potential pregnancies as soon as possible in patients currently on methimazole and propylthiouracil and evaluate the risk of withholding any antithyroid medication during the first trimester against the risk of thyroid storm.
- ☛ **For patients requiring therapy, several expert committees recommend the use of propylthiouracil (PTU) through 16 weeks of pregnancy, followed by transitioning to methimazole for the 2nd & 3rd trimesters.**
 - » Agranulocytosis, liver injury (Jaundice, liver failure), and aplastic anemia are rare but serious complications in patients treated with antithyroid drugs.
 - » If such conditions develop, immediately discontinue the medication and obtain obstetrical consultation.

HYPOTHYROIDISM IN PREGNANCY



- Hypothyroidism in pregnancy is uncommon, because untreated hypothyroidism is associated with infertility. The incidence of hypothyroidism during pregnancy is estimated to be 0.3% to 0.5% for overt hypothyroidism and 2% to 3% for subclinical hypothyroidism. Overt hypothyroidism is defined as thyroid hormone deficiency with low FT4 and elevated TSH levels, whereas subclinical hypothyroidism refers to asymptomatic individuals with elevated TSH and normal FT4 levels.
- Worldwide, the most common cause of hypothyroidism is iodine deficiency. In iodine-sufficient regions, the most common causes are autoimmune thyroiditis and iatrogenic hypothyroidism after treatment for hyperthyroidism. Symptoms such as fatigue, weight gain, decreased exercise capacity, and constipation are often confused with common symptoms of pregnancy; other symptoms such as hair loss, dry skin, and bradycardia may be evident only in more symptomatic persons.
- Overt and subclinical hypothyroidism have been associated with adverse effects on pregnancy and fetal development. These maternal conditions contribute to an increased risk of adverse neonatal outcomes, including preterm birth, low birth weight, and increased perinatal morbidity and mortality. Childhood neurodevelopment also seems to be contingent on thyroid hormone regulation; impairment of neuropsychologic developmental indices and school learning abilities has been noted in children whose mothers had poorly controlled hypothyroidism during pregnancy.
- Clinical features:** Presentation may be asymptomatic or include disproportionate weight gain, lethargy, weakness, constipation, carpal tunnel syndrome, cold sensitivity, hair loss, dry skin, and eventually myxedema.
- Diagnostic workup** same as in nonpregnant patients, but nuclear medicine thyroid scan is contraindicated.



- Levothyroxine is the mainstay of treatment for maternal hypothyroidism.
- Treatment is initiated if thyroid function testing is consistent with hypothyroidism, regardless of symptoms.
- Thyroxine replacement is based on the patient's clinical history and laboratory test values and adjusted until TSH remains normal and stable.
- Tab. Levothyroxine 50mcg or 75mcg or 125mcg (Thyronine)** at dose is 50-150mcg/day (or 2-2.4 mcg/kg/day).
- Monitoring:** Measurement of serum TSH at 4-6 weeks' gestation, then every 4-6 weeks until 20 weeks' gestation and on stable medication dosage. Then again at 24-28 weeks' and 34-38 weeks' of gestation. Stable patients can be tested every trimester. In order to keep serum TSH, serum FT4 or FT4 values within the normal range, the dose need to be increased in the second trimester of pregnancy. After delivery, dose is reduced.
- Treatment goal:** Serum TSH < 2.5 mIU per L.
- Alternative: Thyroxin sodium 5mcg or 100mcg (Thyroxin, Eltroxin)**
Levothyroxine is a synthetic version of a hormone called thyroxine.

Adjustment of Levothyroxine Dosage Based on Thyroid-Stimulating Hormone Level

Serum Thyroid stimulating hormone (TSH) level	Levothyroxine dosage increase
5 to < 10 mIU/L	25 to 50 mcg/day
10 to 20 mIU/L	50 to 75 mcg/day
>20 mIU/L	75 to 100 mcg/day

- Untreated hypothyroidism in early pregnancy has a high fetal wastage in the form of abortion, miscarriage, stillbirth and prematurity and deficient intellectual development of the child. However, pregnancy complications like pre-eclampsia and anemia are high.
- Iodine 131 thyroid ablation is contraindicated in pregnancy.



NORMAL PREGNANCY

Gravidity, Parity, and Duration of Pregnancy

Gravidity: The total number of times a woman has been pregnant, regardless of the outcome.

- **Nulligravidity:** No history of pregnancy
- **Primigravidity:** History of one pregnancy
- **Multigravidity:** History of two or more pregnancies

Parity: The number of pregnancies carried beyond 20 weeks of gestation that result in the birth of an infant weighing more than 500 grams.

- **Nulliparity:** No history of a completed pregnancy that reached beyond 20 weeks' gestation or ended with a birth weight of more than 500 grams.
- **Primiparity:** History of one completed pregnancy that reached beyond 20 weeks' gestation or ended with a birth weight of more than 500 grams.
- **Multiparity:** History of more than one pregnancy that reached beyond 20 weeks' gestation or ended with a birth weight of more than 500 grams.

Fetal age

- **Gestational Age:** Estimated fetal age (in weeks and days) calculated from the first day of the last menstrual period.
- **Conceptional Age:** The age (in weeks and days) of the fetus calculated from the day of conception (fertilization).

Duration of pregnancy

- **Normal duration of pregnancy:** 40 weeks (280 days)
- **Postterm pregnancy:** a pregnancy that extends beyond 42 weeks' gestation or the estimated date of delivery plus 14 days
- **Periviable birth:** live birth occurring between 20–25 weeks of pregnancy
- **Preterm birth:** live birth before the completion of 37 weeks (< 37 0/7) of pregnancy
- **Postterm birth:** live birth after 42 weeks (> 42 0/7) of pregnancy

Trimesters of pregnancy

- First trimester (weeks 1–13)
- Second trimester (weeks 14–26)
- Third trimester (weeks 27–40)

Clinical Relevance

- **Assessment:** Use gravidity and parity to assess obstetric history and manage risk factors.
- **Monitoring:** Track fetal age to determine appropriate timing for prenatal tests and interventions.
- **Adjust management plans** based on the duration of pregnancy and trimester-specific needs.

Pregnancy – Preconception counseling



General principles

- Fertile women of reproductive age should be asked about their intention to become pregnant by their healthcare provider (all those planning to become pregnant should receive counseling).
- **Preconception counseling aims to:**
 - » Identify and address any modifiable factors that may negatively affect pregnancy and childbirth.
 - » Educate women and men about options for risk reduction and elimination.

Patient medical history

1. **Medical conditions:** Review history and identify chronic medical conditions that may affect pregnancy (e.g., Hypothyroidism, Diabetes mellitus, Chronic hypertension)
 - **Hypothyroidism**
 - » Screen women with a desire to conceive with risk factors for thyroid disease (e.g., age > 30 years, obesity, history of head or neck radiation).
 - » Treat women with a desire to conceive with ↑ TSH with **Levothyroxine** until TSH levels are normal.
 - **Diabetes mellitus**
 - » Educate affected women about the importance of maintaining normal blood sugar levels before and during pregnancy.
 - » Assess for complications of diabetes (e.g., Retinopathy, Nephropathy).
 - » **Aim for an HbA1c level < 6.5%.**
 - **Hypertension**
 - » Assess for retinopathy, renal disease, and ventricular hypertrophy.
 - » **Avoid using ACE inhibitors** (Captopril, Enalapril) and **ARBs** (Losartan), as they are teratogenic.
2. **Family history of inherited conditions:** Assess family history of genetic conditions and cancer (e.g., Breast CA, Endometrial CA, and Colon CA) and refer couples with a positive history for counseling.
3. **Communicable diseases**
 - **HIV-infection**
 - » **Screen all women for HIV.**
 - » Initiate antiretroviral therapy in all women with HIV.
 - » Counsel women with HIV regarding the risk of vertical transmission.
 - **Other infections:** STIs, HBV, HCV, TB (screen women at high risk and manage as appropriate)
4. **Medications**
 - Review current medications, including alternative medicine preparations (e.g., herbal medicine, naturopathy) and nutritional supplements.
 - **Discontinue teratogenic drugs** and **switch to safer medications**, if possible.
 - Adjust the regimen of necessary medications and consider using the lowest dose possible for potentially harmful agents.
5. **Immunizations and pregnancy**
 - **Before pregnancy**
 - » Measles, Mumps, Rubella (MMR vaccine), and Varicella vaccine
 - Screen all women for immunity with antibody titers.
 - Non-immune women should receive vaccination.
 - Counsel to avoid conceiving for 28 days after the last vaccine dose.
 - **During pregnancy**
 - » **Influenza:** Women who wish to conceive should receive the annual inactivated influenza vaccine.
 - » **Tetanus, diphtheria, and pertussis (Tdap vaccine):** Women who wish to conceive should receive the Tdap vaccine according to the guidelines.
 - » **Hepatitis B vaccine:** Vaccinate women with high risk for hepatitis-B.
6. **Mental disorders**
 - Review history of psychiatric disorders.
 - Inform about the risks of medication during pregnancy.
 - Screen women with no history of mental health conditions for anxiety and depression.



Counselling – Lifestyle modifications during pregnancy

- ☛ Recommend maintaining a normal body weight prior to conception.
- ☛ Encourage regular moderate-intensity exercise.
- ☛ **Nutrition**
 - » Screen for sufficient intake of macronutrients and micronutrients (calcium, iron, vitamin B12, vitamin B, and vitamin D).
 - » Ensure **vitamin-A** is not taken in excess
 - » Recommend intake of **0.4 mg of folic acid daily**, ideally 4 weeks prior to conception, and continue for at least the first 2–3 months of pregnancy.
- ☛ **Substance use**
 - » Screen all women for alcohol, tobacco, and recreational drug use.
 - » Educate about associated adverse effects of substance use on maternal and fetal pregnancy outcomes.
 - » Provide assistance and/or refer to the proper specialists for tobacco, alcohol, and recreational drug use cessation.

Management of exposures

- ☛ **Exposure to harmful agents**
 - » Advise patients to assess workplace and household for potentially harmful agents (e.g., heavy metals, solvents, chemicals).
 - » Educate the patient about the avoidance of harmful agents and refer them to occupational medicine programs as needed.
- ☛ **Exposure to violence**
 - » Screen for family violence at each visit.
 - » **If ongoing abuse is identified, providers should:**
 - Provide community resources to the patient
 - Report the case as appropriate

Clinical signs of early pregnancy

A. Presumptive signs

1. **Amenorrhea:** absence of menstruation
2. Nausea and vomiting
3. Breast enlargement and tenderness
4. **Linea nigra:** darkening of the midline skin of the abdomen
5. Hyperpigmentation of the areola
6. Abdominal bloating and constipation
7. Increased weight gain
8. Cravings for or aversions to certain foods
9. Increased urinary frequency
10. Fatigue

B. Probable signs

Signs	Physical findings	Weeks of Pregnancy
Goodell sign	Cervical softening	First 4 weeks
Hegar sign	Softening of the lower segment of the uterus	Between 6–8 weeks
Ladin sign	Softening of the midline of the uterus	First 6 weeks
Chadwick sign	Bluish discoloration of vagina and cervix	Between 6–8 weeks
Telangiectasias and palmar erythema	Small blood vessels and redness of the palms	First 4 weeks
Chloasma	Hyperpigmentation of the face (forehead, cheeks, nose)	First 16 weeks

Diagnosis of Pregnancy: Clinical Guidelines

HUMAN CHORIONIC GONADOTROPIN (hCG)

- Site of production: Placental syncytiotrophoblast
- Structure:
 - » α -subunit: common to hCG, FSH, LH, and TSH
 - » β -subunit: Specific to the placenta (pregnancy tests measure the β -hCG levels)
- Function
 - » Maintenance of the corpus luteum during the first 8–10 weeks of pregnancy (LH has a similar function)
 - » Luteal-placental shift: Levels decrease after corpus luteum involution (placenta starts synthesizing its own estriol and progesterone)
- Pregnancy test: Measurement of human chorionic gonadotropin (β -hCG)
 - » Urine β -hCG test: Detects human chorionic gonadotropin (hCG) in urine.
 - Qualitative test; Sensitivity: Less sensitive than serum pregnancy test, Reliable from the first day of a missed period, with high accuracy when performed correctly.
 - β -hCG can be detected in urine 14 days (2 weeks) after fertilization
 - » Serum β -hCG test: Blood test to detect and measure levels of Hcg – Best test
 - Types:
 1. Qualitative Test: Confirms the presence of hCG.
 2. Quantitative Test (high sensitivity): Measures the concentration of hCG, useful for assessing gestational age and detecting abnormal pregnancies.
 - Detectable 6–9 days (on average) after fertilization

OVERVIEW OF HUMAN CHORIONIC GONADOTROPIN (β -hCG)

β -hCG findings	Description	
Normal	β-hCG concentration doubles every 2.5 days for the first 4 weeks of pregnancy. • β-hCG peaks at 8–10 weeks of gestation (Peak value = 100,000 mIU/mL) • β-hCG decreases during the second trimester • β-hCG reaches a steady level during the third trimester • At β-hCG level of 1,500–2,000 mIU/mL the gestational sac will be visible with transvaginal ultrasound (if β-hCG < 1000 mIU/mL, Repeat β-hCG and transvaginal ultrasound after 2–3 days)	
Low	Maternal (mother side) • Ectopic pregnancy • Abortion	Fetal (baby side) • Edwards syndrome • Patau syndrome
High	Maternal • β-hCG secreting tumors » Hydatidiform mole » Choriocarcinoma » Multiple pregnancies	Fetal • Down syndrome
False Positive	• Recent mononucleosis infection • IgA deficiency: due to heterophilic antibody formation » Antibodies cross-react with serum beta-hCG test » Urine β-hCG test should be performed as antibodies do not cross the glomerular membrane.	



USG, GESTATIONAL AGE & EDD IN PREGNANCY

Ultrasound (Abdominal or Transvaginal) findings in normal pregnancy

- ☞ Confirms pregnancy
 - » At 5th weeks of pregnancy: Detection of the gestational sac (corresponds with a serum β -HCG level of 1500–2000 mIU/mL)
 - » At 5–6 weeks of pregnancy: Detection of the yolk sac
 - » At 6–7 weeks of pregnancy: Detection of the fetal pole & cardiac activity with transvaginal ultrasound
 - » At 10–12 weeks of pregnancy: Detection of fetal heartbeat with doppler ultrasound
 - » At 18–20 weeks of pregnancy: Fetal movements

Gestational Age and Estimated Date of Delivery (EDD)

- ☞ Naegele rule: used to calculate the expected date of delivery (due date)
 - » First day of the last menstrual period + 7 days + 1 year - 3 months
 - » Inaccurate if:
 - The date of the last menstrual period is uncertain or unknown
 - The patient has irregular menstruation cycles
 - The patient conceived while taking contraceptive pills
- ☞ Ultrasonography
 - » More accurate than Naegele rule
 - » Measurement of the crown-rump length (CRL) in the first trimester
 - » Measurement of bi-parietal diameter, fetal femoral length, and abdominal circumference in the second and third trimesters (can be used for determining gestational age starting at 13 weeks)
- ☞ Symphysis fundal height: the length from the top of the uterus to the top of the pubic symphysis
 - » Used to assess fetal growth and development from approx. 20 weeks' gestation onwards
 - » Development is approx. 1 cm/week after 20 weeks
 - » Correlates with gestational age

PHYSIOLOGICAL CHANGES DURING PREGNANCY

1. Cardiovascular system

- ☞ $\uparrow$ Progesterone $\rightarrow$ $\downarrow$ vascular tone $\rightarrow$ $\downarrow$ peripheral vascular resistance ($\downarrow$ afterload)
 - » $\uparrow$ Cardiac output by up to 40% ($\uparrow$ preload)
 - » $\uparrow$ Stroke volume (by 10 – 30%)
 - » $\uparrow$ Heart rate (by = 12 – 18 bpm) $\rightarrow$ $\uparrow$ uterine perfusion
 - » $\downarrow$ Mean arterial pressure (MAP)
- ☞ Innocent systolic murmur
- ☞ The apex beat is displaced upward.
- ☞ $\uparrow$ Plasma volume $\rightarrow$ $\downarrow$ oncotic pressure $\rightarrow$ edema of lower limbs
- ☞ Varicosities
- ☞ Aggravation of preexisting valvular diseases

2. Respiratory system

- ☞ $\uparrow$ Oxygen consumption (by approximately. 20%)
- ☞ $\uparrow$ Intraabdominal pressure through uterine growth $\rightarrow$ dyspnea (the diaphragm is displaced upwards $\rightarrow$ $\downarrow$ total lung capacity, residual volume, functional residual capacity, and expiratory reserve volume)
- ☞ Progesterone stimulates the respiratory centers in the brain $\rightarrow$ hyperventilation (to eliminate fetal CO₂ more efficiently) $\rightarrow$ physiological, chronic compensated respiratory alkalosis
 - » $\uparrow$ Tidal volume $\rightarrow$ $\uparrow$ minute ventilation
 - » $\downarrow$ PCO₂ (~ 30 mm Hg)

3. Renal system

- ☞ $\uparrow$ Renal plasma flow $\rightarrow$ $\uparrow$ GFR $\rightarrow$ $\downarrow$ BUN and creatinine
- ☞ $\uparrow$ Aldosterone $\rightarrow$ $\uparrow$ plasma volume and hyponatremia



- ☞ ↑ Progesterone and intraabdominal pressure → dilation of kidney, pelvis, and calyceal systems → reduced tone and peristalsis
 - » Hydronephrosis and hydroureter
 - » Urinary stasis → pyelonephritis
 - » ↑ Urinary frequency
- ☞ ↑ **Glucose levels in urine:** Increased glomerular filtration results in overload of the glucose carrier responsible for its resorption.
- ☞ **Mild proteinuria:** Increased GFR and glomerular permeability to albumin increases protein excretion.
- 4. Endocrine system**
 - ☞ **Progesterone**
 - » Responsible for pregnancy maintenance
 - » Produced by the corpus luteum until the 10–12 weeks of gestation, after which it is produced by the fetoplacental unit
 - ☞ **Human Placental Lactogen:** a hormone synthesized by syncytiotrophoblasts of the placenta, which promotes the production of insulin-like growth factors.
 - » Increases insulin levels
 - » Causes insulin resistance
 - » Increases serum glucose levels and lipolysis to ensure sufficient glucose supply for the fetus
 - » Maternal insulin resistance begins in the second trimester and peaks in the third trimester.
 - ☞ **Thyroid Hormones**
 - » ↑ hCG → ↓ TSH levels during the first part of the first trimester
 - » ↑ TBG → ↑ T4 and T3 → slightly increased free T4 and T3 levels during first trimester
 - » Free T4 and T3 levels decrease during the second and third trimesters
 - ☞ ↑ SHBG and corticosteroid-binding globulin
 - ☞ ↑ Triglycerides and cholesterol (due to increased lipolysis and fat utilization)
 - ☞ Hyperplasia of lactotroph cells in the anterior pituitary → physiological enlargement of the pituitary gland (up to 40% increase from pregestational volume)
- 5. Hematologic system**
 - ☞ ↑ Plasma volume → ↓ hematocrit, especially towards the end of pregnancy (30 – 34th week of gestation) → dilutional anemia (hemoglobin value rarely drops below 11 g/dL)
 - ☞ ↑ RBC mass (increases from 8 – 10th week of gestation until the end of pregnancy)
 - ☞ ↓ Platelet count
 - ☞ ↑ WBC count
 - ☞ ↓ Albumin
 - ☞ Hypercoagulability is due to an increase in fibrinogen, factor VII, and factor VIII and a decrease in protein S; (reduces the risk of intrapartum blood loss).
 - ☞ ↑ Alkaline phosphatase (Placental Isoenzymes)
 - ☞ ↓ Iron and folate levels due to increased vitamin and mineral requirements
- 6. Gastrointestinal system**
 - ☞ ↑ Salivation
 - ☞ ↓ Lower esophageal sphincter tone → gastroesophageal reflux
 - ☞ ↓ Motility → constipation
 - ☞ Gallbladder stasis → gallstones
 - ☞ Hemorrhoids
- 7. Musculoskeletal system**
 - ☞ **Pelvic girdle pain**
 - » **Etiology:** increased pressure from the uterus, lumbar lordosis, and relaxation of the ligaments supporting the joints of the pelvic girdle
 - » **Clinical features:** lower back pain
 - Particularly between the posterior iliac crest and the gluteal fold and in the area of the sacroiliac joint
 - May radiate to the thighs and hips
 - Worsens with weight-bearing



- » **Diagnosis:** positive pelvic pain provocation tests (e.g., posterior pelvic pain provocation test, FABER test, active straight leg raise)
- » **Management**
 - **Nonpharmacological:** heat therapy, manual therapy (e.g., massage, spinal manipulation), braces, physical therapy
 - **Pharmacological:** Tab. Paracetamol 500mg
- ☞ **Round ligament pain**
 - » **Etiology:** stretching of the round ligament of the uterus as the uterus expands
 - » **Epidemiology:** one of the most common conditions during pregnancy
 - » **Clinical features**
 - Typically manifests in the second and third trimester
 - Sharp pain in the lower abdomen and groin area (most often right-sided)
 - Triggered by sudden and/or rapid movements (e.g., rolling over in bed, sneezing, vigorous physical activity)
 - » **Diagnosis:** based on clinical history
 - » **Management:** usually no treatment required; resolves after delivery
- 8. **Skin**
 - ☞ Spider angioma
 - ☞ Palmar erythema
 - ☞ **Striae gravidarum:** scarring that manifests as erythematous, violaceous, and/or hypopigmented linear striations on the abdomen
 - ☞ **Hyperpigmentation:** chloasma, linea nigra, hyperpigmentation of the nipples
 - ☞ Linea nigra and polymorphic eruption of pregnancy
- 9. **Reproductive system**
 - ☞ **Uterus:** increase in size
 - ☞ **Vulva and vagina**
 - » Vaginal discharge
 - » Formation of varicose veins
 - ☞ Mammary glands increase in size

NUTRITION DURING PREGNANCY

- ☞ **Nutritional intake:** Must be adapted to meet the demands of both the mother and the fetus
- ☞ **Dietary recommendations**
 - » **Limit caffeine intake:** Daily recommended dose < 200 mg (This equals about 1–2 cups of coffee or 2–4 cups of caffeinated tea)
 - » Avoid alcohol and tobacco use throughout pregnancy.
 - » Avoid unwashed or uncooked foods.
 - **Fish** (Contamination with parasites and bacteria)
 - **Milk products:** High risk of congenital listeriosis
 - **Meat:** High risk of congenital toxoplasmosis
 - » Avoid fish with possibly high levels of methylmercury, esp. tilefish, swordfish, mackerel, and tuna.

Recommended vitamin and mineral supplementation in pregnancy

- ☞ **Folic acid:** 0.4–0.8mg/day, ideally, women should begin intake 4 weeks prior to pregnancy and continue with this dose for at least the first 2–3 months of pregnancy.
- ☞ **Vitamin B12:** 2.6 mcg/day, Recommended for pregnant women who follow a vegan diet
- ☞ **Iron:** 30–60 mg/day
- ☞ **Calcium:** 1,000–1,300 mg/day
- ☞ **Iodine:** 250 µg/day

Recommended weight-gain during pregnancy

- ☞ **Recommended weight-gain is determined by body mass index (BMI) prior to pregnancy**
 - » **BMI < 18.5 (underweight):** 28 – 40 lb (12–18 kg)
 - » **BMI 18.5–24.9 (normal weight):** 25 – 35 lb (11–16 kg)
 - » **BMI 25–29.9 (overweight):** 15 – 25 lb (7–11 kg)
 - » **BMI ≥ 30 (obese):** 11 – 20 lb (5 – 9 kg)
- ☞ **Average recommended daily calorie intake**
 - » **First trimester:** 2,200 kcal
 - » **Second and third trimester:** 2,500 kcal
- ☞ Regular physical activity is recommended (see below)



PHYSICAL ACTIVITY DURING PREGNANCY

- ☛ Regular physical activity (aerobic and strength-training exercise) is considered beneficial and is recommended before, during, and after pregnancy.
- ☛ Careful evaluation of medical and obstetric disorders is necessary before recommending regular physical activity.
- ☛ **Contraindications to aerobic exercise**
 - » Severe anemia
 - » Restrictive lung disease
 - » Hemodynamically significant heart disease
 - » Cervical insufficiency
 - » Premature rupture of membranes
 - » Gestational hypertension and preeclampsia
- ☛ Exercise routines that are considered unsafe during pregnancy should be avoided or modified accordingly.

SAFE AND UNSAFE SPORTS DURING PREGNANCY

Safe activities	☛ High impact training » Running, jogging » Racquet sports » Strength training ☛ Low impact training » Swimming » Walking » Stationary cycling » Pilates and Yoga
Unsafe activities	☛ Contact sports (e.g., soccer, basketball) ☛ Activities associated with a high risk of falling (e.g., snow and water skiing, gymnastics, surfing) ☛ Activities associated with high risk of dehydration (e.g., hot yoga, hot pilates) ☛ Extreme sports (e.g., skydiving, scuba diving)

HIGH-RISK PREGNANCY

Early identification of high-risk pregnancies is vital in order to prevent the occurrence of maternal and fetal complications. They require regular prenatal care to monitor and support the pregnant mother

Risk factors for a complicated pregnancy

- ☛ Family history (medical and obstetric) of complicated pregnancies
- ☛ Personal history
 - » Advanced maternal age (> 35 years)
 - » First pregnancy
 - » Multiple pregnancies
 - » Multiparity (> 5 births)
 - » **Medical conditions** (e.g., antiphospholipid syndrome, hypertension, diabetes mellitus, epilepsy, malignancies)
 - » Social and environmental factors (e.g., drug use, stress)
 - » Preexisting gynecological conditions (e.g., uterine leiomyoma, history of uterine surgery)
 - » **Prior complicated pregnancies**
 - Premature delivery (<38 weeks), baby with low birth weight, or a baby born with congenital defects
 - Prior cesarean delivery
 - Rhesus incompatibility
 - History of >2 abortions or placental abruption
 - **Use of assisted reproductive technologies:** in vitro fertilization, ICSI
 - » Complications that arise during pregnancy



RH INCOMPATIBILITY

- ☛ **Definition:** Rh incompatibility occurs in an Rh-negative mother carrying an Rh-positive fetus. If the mother is exposed to the paternally derived Rh antigens on fetal red blood cells (RBCs) she can become sensitized and produce immunoglobulin-G (IgG) antibodies, usually against the RhD antigen. These maternally derived antibodies can then freely cross the placenta, binding to and destroying fetal RBCs. This is a leading cause of hemolytic disease of the fetus and newborn (HDN or HDFN, also known as erythroblastosis fetalis), which involves progressive fetal anemia, and, if untreated, may ultimately lead to hydrops fetalis (collection of fluid in serous compartments) and death. Survival rates are more than 90%.
- ☛ **Risk factors (Sensitizing events):** History of a Rh-positive fetus to an Rh-negative mother; invasive fetal procedures; medical or surgical termination of first trimester of pregnancy, second trimester MTP, fetomaternal hemorrhage; placental trauma; abortion (spontaneous, threatened, or induced abortion), omission (or inadequate dosing) of appropriate Rh immunoprophylaxis, external cephalic version, ectopic pregnancy, vesicular mole (especially partial mole), twin pregnancies and multiparity.
- ☛ **Clinical classification**
 - » Rhesus-D (Rh-D) red blood cell (RBC) alloimmunization
 - » Hemolysis caused by Rh-D antigen
 - » Non-Rh-D RBC alloimmunization
 - » Hemolysis caused by other, atypical RBC antigens (Kell, Rhc, Kidd, Duffy)

Diagnostic approach

- ☛ In Rh-negative pregnant women, where Rh paternal phenotype is positive or unknown, the possibility of them becoming alloimmunized and producing red cell antibodies should be considered. Laboratory testing for the presence of red cell antibodies is confirmatory.
- ☛ **Screening:** At the first prenatal visit, ABO blood type, RhD type, and red blood cell (RBC)-antibody screening is recommended for all pregnant women (D-negative or D-positive) and repeated RhD-antibody testing for all unsensitized RhD-negative women is also recommended at 24 to 28 weeks' gestation, unless the biologic father is known to be RhD-negative.
- ☛ **History and physical examination:** Rh-negative mothers that have become sensitized to the D antigen may have been exposed to the D antigen in many ways. Taking a detailed history may reveal potential sensitizing events/Presence of risk factors
- ☛ **Investigations:**
 - » **ABO and Rh typing of the mother**
 - ☛ Rh-positive mothers do not need further screening.
 - ☛ Rh-negative mothers: All Rh-negative pregnant women are at potential risk for alloimmunization and erythroblastosis. screening for anti-D antibodies (mother serum antibody screen & titer)
 - **No anti-D antibodies (unsensitized mothers):** antibody screening repeated at 28 weeks' gestation and at delivery.
 - Anti-D antibodies manifest with an anti-D antibody titer $>1:8$, which indicates maternal sensitization to fetal Rh antigens (sensitized mothers). Further monitoring with amniocentesis & radiological test (Fetal USG, Cerebral Artery Doppler) is required for evidence of hemolysis.
 - **Fetal USG:** may show subcutaneous edema, ascites, pleural effusion, or pericardial effusion
 - **Doppler velocimetry of fetal middle cerebral artery (peak systolic velocity):** ≥ 1.5 MoM
 - **Direct assessment of fetal anemia [through umbilical cord venipuncture (cordocentesis) or the intrahepatic vein]:** Fetal hemoglobin and hematocrit
 - » **Fetomaternal hemorrhage in Rh-negative mother:** Rosette test, Kleihauer-Betke test
 1. **Conduct a rosette test (initial test of choice):** This is a qualitative test that assesses whether fetomaternal hemorrhage (FMH) has occurred.
 - ☛ The apt test is an alternative to the rosette test, but it only differentiates whether the origin of blood is fetal/newborn or from the mother, e.g., from:
 - Newborn gastrointestinal (stool, vomiting) or pulmonary bleeding
 - Antepartum hemorrhage (e.g., vasa previa)



2. If the rosette test is positive, conduct a Kleihauer-Betke test (FMH test).
 - ↳ Quantitative testing to evaluate fetomaternal hemorrhage (measure the amount of fetal blood in the maternal circulation).
 - ↳ The amount of fetal hemoglobin determines the amount of Anti-D immunoglobulin necessary.
 - ↳ Flow cytometry is an alternative, but its use is limited by equipment and costs.
- ↳ Fetal blood grouping (from amniocentesis or maternal circulation): Rh type
- ↳ Father (Paternal) blood testing:
 - ↳ Paternal (father) blood grouping: Rh-Positive – (An Rh-positive partner of an Rh-negative mother creates blood group incompatibility in the fetus).
 - ↳ Paternal zygosity: homozygous or heterozygous (determined by assay of plasma DNA in the case of RhD; serologic testing of father RBCs can be used for analysis of other red cell antigen systems)



TREATMENT OF RH INCOMPATIBILITY

Prevention of Rh incompatibility

- ↳ Premarital counselling
- ↳ Proper matching of blood particularly in women before childbearing.
- ↳ Blood grouping is a must for every woman, before first pregnancy.
- ↳ Rh +ve Blood transfusion-300mcg Immunoglobulin (minimum).
- ↳ Proper management of unsensitized Rh negative pregnancies.

Unsensitized RhD-negative mother → Routine Antenatal Anti-D Prophylaxis (RAADP)

- ↳ Anti-D immunoglobulin (RhoGAM) at dose 300mcg (1500 IU) at 28 weeks' gestation and within 72 hours following the birth of a Rh-positive baby (fetal blood type is unknown or known to be Rh-positive), recommended by the American College of Obstetricians and Gynecologists, and the US Preventive Services Task Force.
- ↳ Dosage of Anti-D immunoglobulin (RhoGAM)
 - ↳ Standard dose: 300 mcg (1500 IU) x IV/IM
 - ↳ If whole fetal blood is > 30 mL (i.e., fetal RBCs > 15 mL): 300 mcg (1500 IU) IM should be given for every 30 mL of fetal blood volume.
 - ↳ Adjusted dose in the first trimester: 50–120 mcg

Further indications of Anti-D immunoglobulin (RhoGAM) in Rh negativity

Potentially sensitizing events

1. Following a miscarriage/abortion, or termination of pregnancy
2. Bleeding during pregnancy/abdominal trauma in pregnancy
3. Ectopic pregnancy, molar pregnancy/vesicular mole (especially partial mole)
4. Following invasive procedures (e.g., chorionic villus sampling, amniocentesis)
5. External cephalic version (ECV) in breech presentation

↳ First 12 weeks of gestation: Anti-D immunoglobulin (RhoGAM) at dose of 50 mcg (250 I.U) given, as soon as possible after the potentially sensitizing events as listed above in first 12 weeks.

↳ 12 to 20 weeks of gestation for potentially sensitizing events: Anti-D at dose of 50 mcg (250 I.U)

↳ 20 weeks of gestation to term for potentially sensitizing events irrespective, Routine antenatal anti-D prophylaxis (RAADP) has been given: Advice Kleihauer-Betke test and immediate administer Anti-D immunoglobulin (RhoGAM) at dose 100 mcg (500 I.U) within 72 hours of event

↳ Does the Kleihauer-Betke test (FMH test) indicate that further anti-D is required??

↳ Administer more anti-D following discussion with specialist.

↳ At delivery (or on diagnosis of intrauterine fetal death >20 weeks):

↳ As the baby's group confirmed as RhD positive? OR are cord samples not available?

↳ Advice Kleihauer-Betke test and immediate administer Anti-D immunoglobulin (RhoGAM) at dose 100 mcg (500 I.U) within 72 hours of event.

↳ Sensitized RhD-negative mother: If antibody screening identifies anti-D antibodies in an RhD-negative pregnant woman, and assessments conclude that their presence is active, not passive, the patient should be considered sensitized, and specialist obstetric advice should be sought.

↳ Rh immunoprophylaxis is no longer given.



ECTOPIC PREGNANCY

Localization	ETIOLOGY	RISK FACTORS
	Anatomic alteration of the fallopian tubes	Non-anatomical risk factors
✓ Fallopian tube (= 95% of cases) ▪ Ampulla (= 70%) ▪ Isthmus (= 15%) ▪ Fimbriae (= 8%) ▪ Interstitial/cornual pregnancy (= 2%): implantation of gestational sac in the cornua of a bicornuate or septate uterus ✓ Ovary (= 3%) ✓ Abdomen (= 1%) ✓ Cervix (< 1%)	✓ History of PID (salpingitis) ✓ Previous ectopic pregnancy ✓ Surgeries involving the fallopian tubes ✓ Endometriosis ✓ Ruptured appendix ✓ Kartagener syndrome ✓ Exposure to diethylstilbestrol (DES) in utero ✓ Bicornuate uterus	✓ Smoking ✓ Advanced maternal age ✓ Pelvic inflammatory disease (PID) ✓ Intrauterine device ✓ In vitro fertilization ✓ Hormone therapy

CLINICAL FEATURES

General Symptoms	Features of Tubal Rupture
✓ Patients usually present with signs and symptoms 4–6 weeks after their last menstrual period. ✓ Lower abdominal pain and guarding (ectopic pregnancy is often mistaken for appendicitis due to the similarity of symptoms) ✓ Possibly, vaginal bleeding ✓ Signs of pregnancy » Amenorrhea » Nausea » Breast tenderness » Frequent urination ✓ Tenderness in the area of the ectopic pregnancy ✓ Cervical motion tenderness, closed cervix ✓ Enlarged uterus ✓ Interstitial pregnancies tend to present late, at 7–12 weeks of gestation, because of myometrial distensibility.	✓ Acute course with sudden and severe lower abdominal pain (acute abdomen) ✓ Signs of hemorrhagic shock (e.g., tachycardia, hypotension, syncope) » In some cases, acute hemorrhage may lead to bradycardia. » The exact mechanism behind this phenomenon is not yet fully understood. ▪ One theory is the activation of mechanoreceptors in the left ventricle that trigger a vagally mediated reflex. ▪ Another suggested cause for bradycardia is a vagally mediated parasympathetic reflex that gets activated by the blood in the peritoneum. ✓ More common in interstitial pregnancy

DIAGNOSTIC APPROACH

- ✓ **Increased Beta Hcg level:** Cutoff is typically beta-hCG > 1,500–2,000 mIU/mL. Multiple pregnancies may have higher beta-hCG levels.
- ✓ **CBC:** Anemia may be seen in patients with vaginal bleeding.
- ✓ **Blood type and screen:** ABO and Rh testing to identify patients who might need Rho immunization
- ✓ **LFT, Basic Metabolic Panel:** to determine baseline liver and renal function
- ✓ **Transvaginal ultrasound (TVUS):** Empty uterine cavity in combination with a thickened endometrial lining
- ✓ **Transabdominal ultrasound (TAUS):** Can be used to exclude differential diagnoses (acute appendicitis)
- ✓ **Exploratory laparoscopy → Indication:** 1. unstable patients suspected of having an ectopic pregnancy.
2. In pregnancy of unknown location if the location is still uncertain after 7–10 days
- ✓ **Endometrial biopsy → Indication:** Consider only in cases of pregnancy of unknown location where non-viability is certain.



MANAGEMENT OF ECTOPIC PREGNANCY

The following recommendations are consistent with the 2018 ACOG practice bulletin on tubal ectopic pregnancy

Approach to the management of ectopic pregnancy

- **OB/GYN consult for consideration of medical treatment, surgical treatment, or expectant management**
- **Unstable patients:** See below "treatment of ruptured ectopic pregnancy."
 - » Begin acute stabilization (ABCD&E approach).
 - » Obtain an immediate OB/GYN consult for emergency surgery.
- **Stable patients:** Determine whether medical, surgical, or expectant management is appropriate.
 - » Consider clinical, laboratory, and radiological findings.
 - » Share decision-making with patients in consultation with OB/GYN.
- **All patients:** Provide adequate supportive care.
- **Patients suited to medical or expectant management at home**
 - » Provide education on red flag symptoms indicating rupture, e.g., severe worsening pain, shoulder tip pain, dizziness, or heavy bleeding.
 - » Arrange appropriate follow-up prior to discharge.
- **Supportive care:** Provide for all patients regardless of management approach.
 - » Provide analgesia for pain relief
 - » Prenatal and contraceptive counseling once treatment is complete
- **For Rh-negative patients who present with bleeding:** administer Anti-D immunoglobulin (RhoGAM) at dose of 50 mcg (250 I.U.) x IV/IM

Medical therapy (methotrexate)

- **Methotrexate (MTX) is the treatment of choice.**
- **Mechanism of action:** inhibits folate-dependent steps in DNA synthesis to terminate the rapidly dividing ectopic pregnancy.
- **Indications of methotrexate**
 - » Uncomplicated ectopic pregnancies
 - » Hemodynamically stable patients
 - » Unruptured mass
 - » β -hCG $\leq$ 2,000 – 5,000 mIU/mL
 - » Mass size $<$ 3.5 cm
 - » No fetal heartbeat

Absolute contraindications of methotrexate

- **Chronic conditions:** Pulmonary (e.g., severe asthma), Renal (creatinine clearance $<$ 50 mL/min/1.73 m²), Hepatic (alcohol use disorder or chronic liver disease), Hematologic (Leukopenia, thrombocytopenia, severe anemia)
- Intrauterine pregnancy
- Breastfeeding
- Methotrexate sensitivity
- Immunodeficiency
- Peptic ulcer disease
- Ruptured ectopic pregnancy

Methotrexate regimens for medical treatment of Ectopic Pregnancy

	Single-dose regimen	Two-dose regimen	Multiple-dose regimen
Characteristics	» Lower risk of adverse effects than other regimens	» More effective than single-dose regimen for patients with high initial β -hCG	» More adverse effects than other regimens » Higher success rate than other available regimens
Methotrexate administration	» Day 1: methotrexate	» Day 1: methotrexate » Day 4: methotrexate	» Days 1, 3, 5, 7: methotrexate » Days 2, 4, 6, 8: Folinic acid
β -hCG monitoring	» β -hCG on day 4 » β -hCG on day 7	» β -hCG on day 4 (after treatment) » β -hCG on day 7	» β -hCG on days of treatment with MTX
Response to β -hCG monitoring results	» Decrease $>$ 15% from day 4 to day 7: Measure β -hCG weekly until negative. » Decrease $<$ 15% from day 4 to day 7: Repeat MTX dose. » No decrease after 2 doses: Consider surgical management.	» Decrease $>$ 15% from day 4 to day 7: Measure β -hCG weekly until negative. » Decrease $<$ 15% from day 4 to day 7: Repeat MTX dose on day 7 and measure β -hCG on day 11. » This may be repeated until the patient has received 4 doses. » No decrease after 4 doses: Consider surgical management.	» Decrease $>$ 15% in 2 consecutive measurements: Discontinue MTX and measure β -hCG weekly until negative. » No β -hCG decrease after 4 doses: Consider surgical management.
Follow up	If β -hCG levels increase or plateau during weekly follow up, consider persistent ectopic pregnancy.		

- **Monitoring of methotrexate Adverse effects**
- **Patients should avoid the following during methotrexate (MTX) therapy:**



- » Exercise and sexual activity
- » Folic acid supplements, foods with a high folic acid content, and NSAIDs
- » Prolonged exposure to sunlight
- » Alcohol and gas-producing foods
- » **Methotrexate (MTX) therapy** is contraindicated in ruptured ectopic pregnancy!

Non-urgent surgical management	Expectant management
» See "treatment of ruptured ectopic pregnancy below" for emergency surgical indications and preferred approach. » Indications for non-urgent surgery » Contraindications for Methotrexate (MTX) » Unsuccessful medical treatment » A concurrent surgical procedure (e.g., bilateral tubal blockage) is necessary. » The patient has indicated a preference for surgical treatment. » Approach Laparoscopy (preferred) » Procedure: Salpingostomy, i.e., removal of ectopic pregnancy without removing the affected fallopian tube (tube-conserving operation) » Preferred in patients with Unruptured tubal pregnancy who do not meet the criteria for conservative treatment » Complications ▪ Risk of persistent ectopic pregnancy ▪ Risk of repeat ectopic pregnancy » Additional considerations ▪ Patients require serial B-hCG measurement. ▪ Consider a prophylactic dose of Methotrexate (MTX) if there is concern for incomplete resection. » Salpingectomy may be required in select cases (e.g., large ectopic mass).	Asymptomatic patients with very low β-hCG levels may experience spontaneous resolution of ectopic pregnancy without medical or surgical treatment. Consider this approach in select patients after consultation with OB/GYN. » Indications » Minimal symptoms » No evidence of ectopic mass on TVUS » Confirmed plateauing or decreasing serial β-hCG levels » Considerations during expectant management » Provide extensive counseling on the risks of complications in addition to general counseling (see "Approach"). » Arrange close surveillance and serial β-hCG measurement (every 2–7 days). » Conversion to medical or surgical therapy » Increasing symptoms, e.g., pain, signs of ruptured ectopic pregnancy » Insufficient decrease, persistent plateau, or increase in β-hCG levels



TREATMENT OF RUPTURED ECTOPIC PREGNANCY

- » **Stabilize the ABCDE approach** for patients with obvious signs of rupture and those at high risk of impending rupture.
- » **Rapid assessment**
 - » **Suspect ruptured ectopic pregnancy in patients in their first trimester with any of the following:**
 - » Clinical features of shock: e.g., tachycardia, hypotension, pallor
 - » Severe abdominal or pelvic pain
 - » Peritoneal signs on examination
 - » Significant vaginal bleeding
 - » POCUS positive for intraperitoneal free fluid
 - » Clinical deterioration after receiving methotrexate (MTX) therapy
- » Obtain emergency OB/GYN consultation without delay if ruptured ectopic pregnancy is likely!
- » **Maintain 2 large bore intravenous line**
- » **NPO the patient**
- » **Start IV fluid resuscitation.**
- » Obtain CBC, blood grouping and screen, and prepared for blood transfusion.
- » **Urgent OB/GYN consult** for emergency salpingectomy
- » **Provide immediate hemodynamic support as needed.**
- » For patients with hemorrhagic shock, start transfusion as soon as blood products are available and consider massive transfusion protocol.
- » **Parenteral analgesics:** Opioids are preferred.
- » Continuous telemetry and frequent blood pressure checks
- » Transfer patient to the OT.

SPONTANEOUS ABORTION



Definition

- Spontaneous abortion: Loss of pregnancy before 20 weeks gestation
- Recurrent pregnancy loss: Two or more miscarriages occurring before 20 weeks gestation

TYPES/CLINICAL FEATURES OF SPONTANEOUS ABORTION

Type	Vaginal bleeding	Fetal activity on USG	Products of conception (POC)	Internal cervical os	Prognosis
Threatened abortion	Yes	Yes	Intrauterine pregnancy	Closed	Reversible
Inevitable abortion	Yes	±	Visible or palpable POC	Open	Irreversible
Missed abortion	No	No	No explosion of the POC	Closed	Irreversible
Incomplete abortion	Yes	No	POC within the cervical canal or uterus	Open	Irreversible
Complete abortion	Yes	Empty uterus	POC completely outside of the uterus	Closed	Irreversible

CLINICAL FEATURES OF SPONTANEOUS ABORTION IN SHORT DETAIL

Threatened abortion: A process of miscarriage that has started but not yet progressed to a state from which recovery is impossible (potentially reversible) before 20 weeks' gestation

Findings:

- » Spotting (vaginal bleed) & Abdominal pain
- » Fetal activity is present
- » On speculum exam: Cervical os - closed

Missed abortion: Death of a fetus before 20 weeks' gestation without expulsion of any POC

Findings:

- » No bleeding or dirty brown discharge
- » No expulsion of the products of conception (POC)
- » No fetal activity
- » On speculum exam: Cervical os - closed

Complete abortion: The complete passage of all POC before 20 weeks' gestation

Findings:

- » Initially vaginal bleeding & abdominal pain
- » When POC comes out then bleeding stops
- » Usually occurs < 12 weeks' gestation
- » On speculum exam: Cervical os - closed

Inevitable abortion: A condition of vaginal bleeding and cervical dilation without expulsion of products of conception (POC) that occurs before 20 weeks' gestation. Typically followed by partial or complete passage of POC

Findings:

- » Vaginal bleeding and abdominal pain
- » Visible or palpable products of conception (POC)
- » Fetus - Live/dead & Cervical os: Dilated (open)

Incomplete abortion: Passage of some but not all products of conception (POC) before 20 weeks' gestation

Findings:

- » Vaginal bleeding and abdominal pain
- » Products of conception (PCO) coming-out through cervical os (PCO within the cervical canal or uterus)
- » Usually occurs > 12 weeks' gestation
- » On speculum exam: Cervical os - Dilated (open)

Stillbirth:

Loss of pregnancy after 20 weeks' gestation (also called intrauterine fetal demise)

Findings:

- » Absence of fetal movements
- » Absence of cardiac activity
- » On speculum exam: Cervical os is variable

DIAGNOSTICS

Doppler ultrasound:

- » Always used to detect fetal heartbeats during prenatal visits.
- » Absence of fetal cardiac activity should raise suspicion of spontaneous abortion.

A Pelvic examination should be performed, in all cases of vaginal bleeding.

In cases of suspected spontaneous abortion:

- » Visualization of the cervix is necessary to confirm that the source of bleeding is uterine.

Transvaginal ultrasound (TVUS):

- » The best test once there is absence of fetal cardiac activity or confirmed uterine bleeding.

Findings consistent with a spontaneous abortion include:

- » Absence of fetal cardiac motion
- » Abnormalities of the yolk sac or gestational sac

Quantitative Beta-hCG Levels: To confirm pregnancy and assess its progression.

CBC: To check for anemia and infection.



Rx

MANAGEMENT OF SPONTANEOUS ABORTION

- Women should be provided with appropriate psychological support and counselling, and they should be provided with information about the likely impact of their treatment on future fertility.
- Initial management should focus on **haemodynamic stabilization** as well as **adequate analgesia**.
- Further management should be based on the presenting symptoms, USG findings, & serum hCG measurements.
- Patient choice should be encouraged at all stages and women should be helped to make informed decisions regarding their own care.
- Prevention: Minimize risk with treatment of maternal disease and adequate prenatal care.
- Expectant management should be offered for 7-14 days as it is the **first-line management** strategy for women with a confirmed diagnosis of miscarriage.
- Threatened abortion
 - » Expectant management: symptoms will resolve or will lead to inevitable/incomplete or complete abortion.
 - » Avoid strenuous physical activity.
 - » Weekly pelvic ultrasound.
 - » Rule out treatable causes of vaginal bleeding; during pregnancy.
 - » Rh (D)-negative women should receive Rh (D)-immune globulin in cases of vaginal bleeding during pregnancy.
- Inevitable abortion, incomplete abortion, or missed abortions: The management of uncomplicated spontaneous abortions depends mostly on patient preference.

Possibilities include:

- » Expectant management; (option for women < 14 weeks gestation): Surgical evacuation is usually recommended if evacuation does not occur after 4 weeks.
- » Medical management
 - Drug of choice: Tab. Misoprostol 200mcg (Cytotec): It is used to induce cervical ripening and expulsion of the POC. Typically, 800 mcg vaginally or orally, may be repeated as needed.
 - Tab. Mifepristone (RU-486): When available, pretreatment with mifepristone 24 hours prior is recommended. Dose 200 mg orally, followed by misoprostol (used less commonly in missed abortion).
- » Surgical management (evacuation of retained products of conception)
 - Preferred method in septic abortion or if there is heavy bleeding or significant maternal disease.
 - Complications include: uterine perforation, hemorrhage, endometritis, and/or intrauterine adhesions.
- » Rh (D) -ve women should receive Rh (D)-immune-globulin in all cases of vaginal bleeding during pregnancy.

Dosage of Anti-D: at <12 weeks = 50 mcg (or 250 I.U) and at ≥12 weeks = 100 mcg (or 500 I.U)

Anti-D is not given in → threatened abortion < 12 weeks, if bleeding is heavy, recurrent or associated with pain. Complete abortion <12 weeks, if any medical/surgical management is not done
- Complete abortion: No treatment required, confirm that the cervical os is closed and that uterus is equal or smaller in size than expected for gestational age.

Surgical Management

- Indicated in cases of heavy bleeding, infection, patient preference, or failure of expectant or medical management.
- Procedures:
 - » Dilation and Curettage (D&C): Surgical removal of uterine contents under local or general anesthesia.
 - » Manual Vacuum Aspiration (MVA): A less invasive suction procedure.
- Effectiveness: Immediate resolution of symptoms and high success rate.
- Complications: Low risk but may include infection, perforation, or anesthesia-related complications.

Supportive Care

1. Emotional Support:
 - » Counseling and support groups for emotional and psychological support.
 - » Open communication with healthcare providers about feelings and concerns.
2. Physical Care:
 - » Pain management with NSAIDs or Paracetamol.
 - » Monitoring for signs of infection, such as fever, increased pain, or foul-smelling discharge.
 - » Iron supplements if significant blood loss occurred.
3. Future Pregnancy Planning:
 - » Discussion about the timing of future pregnancies.
 - » Investigations for recurrent miscarriage if the patient has had multiple miscarriages (e.g., anatomical abnormalities, hormonal imbalances, genetic testing, antiphospholipid syndrome).



RECURRENT OR HABITUAL MISCARRIAGE

- Recurrent or habitual miscarriage is defined as three or more consecutive spontaneous miscarriages, without an intervening live birth. A miscarriage causes a great emotional setback to the woman and her family.
- Most of the pregnancy losses occur before implantation, (approximately 70-75% of the fertilisation), but only 25-30% are clinically recognised. Early pregnancy loss is limited to those pregnancies, which are lost after implantation.
- The incidence of pregnancy loss is increased after each miscarriage. Hence, an endeavour to find out the exact cause is of paramount importance. The risk of spontaneous abortion for a lady with no previous history of abortion is 15%, while the likelihood of repeat abortion after the first pregnancy loss is 20%, which increases with two previous miscarriage to 30-35% and in patients with three previous miscarriage to nearly 50%.
- Prognosis:** The prognosis is excellent if the cause of abortion can be corrected or treated

Etiology of recurrent miscarriage

The exact aetiology is not completely understood, but the following factors are contributory:

- Genetic abnormalities:** 80% of miscarriages in this category occur at less than 8 weeks and are often associated with a blighted ovum. Chromosomal abnormalities most commonly found in miscarriages are:
 - Autosomal trisomy:** Chromosome 16, 21 and 22. The most common is trisomy of chromosome 16, which is due to non-dysjunctional defects.
 - Monosomy X:** mostly Karyotype 45X, many of these are not aborted and present at birth as Turner's syndrome.
- Anatomic abnormalities of the uterus**
 - Congenital defects of uterus:** Müllerian duct abnormalities, defects due to diethyl stilbestrol (DES) exposure in utero, or cervical incompetence. The Müllerian anomalies can involve formation or fusion like septate uterus, bicornuate uterus or unicornuate uterus
 - Acquired defects of uterus:** incompetent cervix, Asherman's syndrome and fibroid uterus
- Endocrine factors:** Progesterone deficiency, Diabetes mellitus, thyroid function abnormalities, Maternal hyperandrogenicity, polycystic ovarian syndrome (PCOS) and Premature ovarian failure
- Infections and chronic diseases**
- Defective placentation:** This type of abnormal placentation is seen in pre-eclampsia, severe IUGR, preterm labour and also in some cases with early foetal deaths
- Immunological causes:** There is an increasing incidence in > 30 years (delayed childbearing in both natural and in vitro fertilisation).
Immunological causes include: Autoimmune factors (Antiphospholipid (APL) antibodies syndrome due to (IgG, IgA or IgM isotopes), Positive antinuclear antibody titers (ANA) and Alloimmune (Immunity against another Person-Foetus and Father) Factors.

DIAGNOSTICS OF RECURRENT MISCARRIAGE

HISTORY TAKING	INVESTIGATIONS
History should include the following points: - Was the pregnancy confirmed by laboratory test or ultrasound (USG)? - What was the duration of amenorrhoea before miscarriages took place? - Was it a genetically normal foetus or congenitally malformed? - Did any cardiac activity appear before bleeding or not? (Any previous ultrasound report) - Was the patient on any kind of prolonged treatment? - Any personal or family history of autoimmune disorder? - Any history of endocrine disorder? - Any history suggestive of a sexually transmitted disease like syphilis? - Any history of Gynaecological procedure undergone, e.g. dilatation and evacuation (D&E)/ dilatation and curettage (D&C), cone biopsy (to rule out cervical incompetence and Asherman's syndrome)? - Any live issues (children) before? - Any history of genetic defects in the partner or family? - Menstrual history, amount and regularity of the menstrual cycle (to rule out PCOD).	Baseline investigations include: - CBC (Hb, WBCs) and ESR Blood sugar level: Fasting & Random level - Blood group and Rh typing - VDRL to rule out syphilis - Urine routine examination for any proteinuria and reducing substances and microscopy Special tests: - Semen analysis for male patient Thyroid profile and Thyroid peroxide antibody - Glycosylated haemoglobin level (HBA1C) - Serum fasting insulin - TORCHS screening Antibodies (Ab) test: Anticardiolipin Ab, Antiphospholipid Ab, Lupus anticoagulant Ab and Anti DNA antibody - Hormone profile (FSH, LH, Prolactin) If a hyperandrogenic state is suspected - Serum total and free testosterone 17-α hydroxy progesterone level - DHEAS levels - Karyotype, USG pelvis/transvaginal - Hysterosalpingography (HSG) and Hysteroscopy - Laparoscopic evaluation of the pelvis & abdomen (optional) - MRI for anatomical defects of the uterus or cervix (optional)



Rx

TREATMENT OF RECURRENT OR HABITUAL MISCARRIAGE

Treatment of specific aetiology

1. First trimester abortions: Find genetic or non-genetic origin
2. Luteal phase defect: Estimation of urinary LH daily will reveal hypersecretion of LH, if present

Assessment of luteal phase is done by:

- » Progesterone level at day 21 (in a 28-day cycle) - less than 10 ng/ml
- » Endometrial histology and dating
- » Serial ultrasound evaluating the endometrium (thickness, echogenicity)
- » Colour Doppler—detection of vascularity

Recommended treatment: Progesterone supplements → Progesterone vaginal pessary/oral gels or Injection. Some clinicians prefer giving **Inj. HCG** (See drug brand section) x weekly or bi-weekly.

However, it has not been seen to be any superior to the progesterone preparation.

- » **Inj. Proluton Depot 250 mg or Inj. Hydroxyprogesterone 250 mg** x Intramuscular (IM) at a dosage of 250 mg (1 mL) once weekly (maximum dosage 250mg to 500mg), in the upper outer quadrant of the gluteus maximus during the first half of pregnancy.
- » Treatment should be initiated **between 16 weeks, 0 days and 20 weeks, 6 days gestation**. Continue administration once weekly until week 37, (through 36 weeks, 6 days) of gestation or delivery, whichever occurs first.
- » OR **Inj. Estradiol 5mg + Progesterone 250mg** (Gravibinan) x intramuscularly (IM) every week during the first months of pregnancy.
- » OR **Cyclogest Pessary 400mg** x per vaginally daily x started periconceptionally (in the luteal phase prior to pregnancy confirmation) till 20 weeks of gestation

Limitations/Exclusions:

Hydroxyprogesterone caproate is not considered a medically appropriate intervention when any of the following are applicable:

- Member must be 16 years of age or older
- Current or history of thrombosis or thromboembolic disorders
- Known or suspected breast cancer, or hormone-sensitive cancer, or history of these conditions
- Undiagnosed abnormal vaginal bleeding unrelated to pregnancy
- Cholestatic jaundice of pregnancy
- Liver tumors, benign or malignant, or active liver disease
- Uncontrolled hypertension

3. PCOS: Pituitary suppression with GnRH analogs followed by ovulation induction (see treatment of PCOS)
4. Hyperandrogenism: Treatment with prednisone
5. Abnormal placentation: Low dose aspirin (Ascard or Loprin) and Dipyridamole
6. Uterine anomalies: Surgery, IVF
7. Immunological causes: Low dose aspirin (Tab. Loprin or Tab. Ascard 75mg) and prednisolone, heparin/LMWH and high-dose intravenous immunoglobulin (IVIG)
8. Antiphospholipid antibody syndrome (APS): Low molecular weight heparin (LMWH) + Low dose aspirin and Low-dose prednisolone is also given if the woman has been diagnosed with systemic lupus erythematosus and not otherwise.
9. Cervical incompetence: Cervical cerclage operation
10. Hyperprolactinaemia: Tab. Bromocriptine 2.5mg to 5mg x daily
 - » Bromocriptine treatment resulted in higher rate of live-births (85.7% vs 52.4% in non-bromocriptine)
 - » Mechanism of hyperprolactinemia: It is thought to suppress the hypothalamic-pituitary-ovarian system leading to insufficient folliculogenesis and oocyte maturation.
11. Vitamins supplementation in women presenting with hyperhomocysteinaemia
 - Tab Methylefolate 400 or 600mcg (Myfol) x OD and Tab. Methylcobalamin 500mcg (Cobalamin) x OD

INDUCED ABORTION (TERMINATION OF PREGNANCY)



DEFINITION

- Induced abortion: The use of interventions (e.g., medications, procedures) to end a pregnancy
- Medication abortion: The administration of medications to end a pregnancy
- Surgical abortion: The physical removal of products of conception from the uterus to end a pregnancy

EPIDEMIOLOGY

Pakistan has an annual abortion rate of 50 per 1,000 women, according to a 2012 survey, the highest in South Asia and one of the highest in world. (27 per 1000 women in 2002.)

ABORTION LAWS IN THE ISLAMIC REPUBLIC OF PAKISTAN

- In Pakistan penal code (Act XLV of 1860): Abortion is referred to as 'Isqat-e-Haml' and 'Isqat-e-Janin' under section 338, 338A, 338B, and 338C.
- Abortion laws in Pakistan's Penal Code are part of the pre-partition laws enacted in 1990 to better align with the Islamic teachings prevalent at the time.
- However, policies in Pakistan favor its illegality, with the exception of cases involving "good faith" only when a woman's life is in danger or "necessary treatment."
- NOW THE QUESTIONS:** Does good faith refers to pregnancy causing physical or mental health disturbance? Financially stability? Pregnancy due to failure of contraceptive methods? Avoiding unwanted pregnancies? Or when pregnancy caused by rap? **SO THE ANSWER:** It probably does not, and even if it does. It doesn't clearly mention in the law so these pregnancies will be consider illegal

1. ILLEGAL ABORTION

- A. **ISQAT-I-HAML 'SECTION-338:** an ending a pregnancy before the child's organs have not formed.

"Whoever causes woman with child whose organs have not been formed, to miscarry, if such miscarriage is not caused in good faith for the purpose of saving the life of the woman, or providing necessary treatment to her, is said to cause isqat-i-hamal."

Explanation: A woman who causes herself to miscarry is within the meaning of this section.

- B. **ISQAT-I-JANIN 'SECTION-338-B':** an ending a pregnancy after the child's organs have fully formed.

"Whoever causes a woman with child some of whose limbs or organs have been formed to miscarry, if such miscarriage is not caused in good faith for the purpose of saving the life of the woman, is said to cause Isqat-i-janin."

Explanation: A woman who causes herself to miscarry is within the meaning of this section.

2. PUNISHMENT FOR ILLEGAL ABORTION UNDER PAKISTAN LAW

- Punishment for Isqat-i-haml 'Section 338- A': Whoever cause isqat-i-haml shall be liable to punishment as ta'zir- (a) with imprisonment of either description for a term which may extend to three years, if isqat-i-haml is caused with the consent of the woman; or (b) with imprisonment of either description for a term which may extend to ten years, if isqat-i-haml is caused without the consent of the woman: Provided that, if as a result of isqat-i-haml, any hurt is caused to woman or she dies, the convict shall also be liable to the punishment provided for such hurt or death as the case may be

- Punishment for Isqat-i-janin 'Section 338- A'

» Whoever causes isqat-i-janin shall be liable to:

- a) one-twentieth of the diyat if the child is born dead;
- b) full diyat if the child is born alive but dies as a result of any act of the offender; and
- c) imprisonment of either description for a term which may extend to seven years as ta'zir:

» Provided that, if there are more than one child in the womb of the woman, the offender shall be liable to separate diyat or ta'zir, as the case may be/for every such child:

» Provided further that if, because of isqat-i-janin, any hurt is caused to the woman or she dies, the offender shall also be liable to the punishment provided for such hurt or death, as the case may be.



3. LEGAL ABORTION → ACCORDING REVISED PRE-PARTITION LAW-1990

- » **Therapeutic:** When the continuation of pregnancy endangers the life of woman or may cause serious injury to maternal health.
For example: Congestive cardiac failure (CCF), Chronic liver diseases (CLD), Chronic renal failure (CRF) and Eclampsia
- » **Eugenic:** When there is risk of the child to be born will suffer from severe mental, physical, structural, **chromosomal** developmental defect.
For example: Down syndrome, Neural tube defect, Beta thalassemia major. Other if the pregnant women in the first three months is suffer from Infectious disease which causes congenital defects [German measles, (incidence of congenital defects 10 to 12%), chicken pox or using of teratogenic drug (Thalidomide, Isotretinoin).

ETHICS IN ABORTION

- ☞ The consent of the woman is required before conducting abortion. Written consent of the guardian is required if the woman is a minor (<18 years) or a mentally ill person. Consent of husband is not necessary.
- ☞ Abortion cannot be performed on the request of the husband, if the woman herself is not willing.
- ☞ The woman need not produce proof of her age. The statement of the woman that she is over eighteen years of age is accepted.
- ☞ Professional secrecy has to be maintained. The Admission Register for the termination of pregnancies is secret document, and the information contained therein should not be disclosed to any person.

PREPARATION OF LEGAL ABORTION

Prior to induced abortion, the following steps should be considered:

- ☞ **Confirm pregnancy:** For example with a urine pregnancy test.
- ☞ Perform a gestational age assessment.
- ☞ **Consider screening ultrasound for patients with:**
 - » Symptoms or risk factors for ectopic pregnancy
 - » History of irregular menstrual cycles
 - » Last menstrual period > 56 days prior (or unknown)
- ☞ **Additional test:** CBC, Blood group with screening for red cell antibodies
- ☞ Use shared decision-making to select the method of induced abortion.
- ☞ **Educate patients on expected symptoms and adverse effects**
For example:
 - » Bleeding and cramping (heavier than menstruation)
 - » GI symptoms: nausea, vomiting, diarrhea
 - » Low-grade fever and chills
- ☞ **Offer additional care as indicated:** E.g. referral for psychosocial services, contraception counseling, screening of sexually transmitted infections (STI).

- ❖ **What to Expect:** Most patients who have a medication abortion will experience bleeding and cramping, which are necessary for the process to occur. Patient counseling should emphasize that bleeding likely will be much heavier than menses (and potentially with severe cramping).
- ❖ **Medication abortion is not recommended for patients with any of the following:** confirmed or suspected ectopic pregnancy, intrauterine device (IUD) in place (the IUD can be removed before medication abortion), current long-term systemic corticosteroid therapy, chronic adrenal failure, known coagulopathy or anticoagulant therapy, inherited porphyria, or intolerance or allergy to mifepristone or misoprostol

Ref: RCOG GUIDELINES

MEDICAL TERMINATION OF PREGNANCY



- 1. Medical abortion at ≤ 9 weeks (≤ 63 days) of gestation (early medical abortion)**
 The following regimens are recommended for early medical abortion:
 at ≤ 9 weeks (≤ 63 days) of gestation: Tab. Mifepristone 200 mg per orally followed 24 to 48 hours later by Tab. Misoprostol 200mcg (Cytotec, Breeky) at dose of 800mcg (4 tablets) has given by the vaginal, buccal or sublingual route.
 at ≤ 7 weeks (≤ 49 days) of gestation: Tab. Mifepristone 200mg per orally followed 24 to 48 hours later by Tab. Misoprostol 200 mcg (Cytotec, Breeky) at dose of 400mcg (2 tablets) per orally
- 2. Medical abortion at 9–13 weeks of gestation**
 The following regimen is recommended for medical abortion between 9 & 13 weeks of gestation:
 Tab. Mifepristone 200mg per orally followed 36 to 48 hours later by Tab. Misoprostol 200mcg (Cytotec, Breeky) at dose of 800mcg (4 tablets) x vaginally. A maximum of 4 further doses of misoprostol 400mcg (4-tablets) may be administered at 3-hourly intervals, vaginally or orally.
- 3. Medical abortion at 13–24 weeks of gestation**
 The following regimen is recommended for medical abortion between 13 & 24 weeks of gestation:
 Tab. Mifepristone 200mg orally, followed 36 to 48 hours later by Tab. Misoprostol at dose of 800mcg (4-tablets) x vaginally, then Tab. Misoprostol 200mcg (Cytotec, Breeky) at dose 400mcg (4-tablets) given 3-hourly, to a maximum of 4 further doses.
 If abortion does not occur, Tab. Mifepristone 200mg can be repeated 3 hours after the last dose of Tab. Misoprostol and 12 hours later Tab. Misoprostol 400mcg (4-tablets) may be recommenced.
 Surgical evacuation of the uterus is not required routinely following medical abortion between 13 and 24 weeks of gestation. It should be undertaken only if there is clinical evidence that the abortion is incomplete.
- 4. Pain relief for medical abortion: NSAIDS = Tab. Naproxen sodium 500mg (Neoprox, Flexin) x Twice daily**
- 5. Rhesus prophylaxis: Inj. Anti-D IgG x IM into the deltoid muscle, should be given to all non-sensitised RhD negative women within 72 hours following abortion, whether by surgical or medical methods.**
- 6. Prophylactic antibiotics: Not recommended for medication abortion**

Ref: ACOG & WHO GUIDELINES

Medical abortion regimens upto 70 days (10 weeks) of gestation

ACOG/WHO REGIMEN

- Day-1: Tab. Mifepristone 200mg x per orally, send her home, follow up after 24-48 hours.
- Day-3: Tab. Misoprostol 200mcg (Cytotec, Breeky) at dose of 800mcg (4 Tablets) x vaginally, sublingually or buccally, then observe for 2-3 hours and send her back home. Follow up after 2 weeks, clinical examination done to as certain complete evacuation.

Alternative Regimen

- Tab. Misoprostol 200mcg (Cytotec, Breeky) at dose of 800mcg (4 Tablets) x vaginally, sublingually or buccally, repeat the dose every 3-12 hrs. for 3 doses. (1st dose of misoprostol 800mcg than 2nd dose 800mcg than 3rd dose of 800mcg)

MEDICAL ABORTION REGIMEN USED IN INDIA

Medical abortion up till 7 weeks of gestation

- Day-1: Tab. Mifepristone 200mg x per orally, send her home, follow up after 24-48 hours.
- Day-3: Tab. Misoprostol 200mcg (Cytotec, Breeky) at dose of 400mcg (2 Tablets) x vaginally, sublingually, then observe for 2-3 hours and send her back home.
- Day-15: Follow up – clinical examination done to as certain complete evacuation.

Medical abortion up till 7 to 9 weeks of gestation

ACOG/WHO REGIMEN

- Day-1: Tab. Mifepristone 200mg x per orally, send her home, follow up after 24-48 hours.
- Day-3: Tab. Misoprostol 200mcg (Cytotec, Breeky) at dose of 800mcg (4 Tablets) x vaginally, sublingually or buccally, then observe for 2-3 hours and send her back home.
- Day-15: Follow up – clinical examination done to as certain complete evacuation.



ANTI-PHOSPHOLIPID SYNDROME (APS)

Definition: Antiphospholipid syndrome (APS) is an autoimmune disease that increases the risk of thrombosis as a result of procoagulatory antibodies. The condition may be idiopathic or acquired secondary to an underlying disease, such as systemic lupus erythematosus. Circulating antibodies deactivate anticoagulatory proteins and activate platelets, thereby inducing a hypercoagulable state.

ETIOLOGY

Primary

- » Idiopathic
- » Associated with genetic marker HLA-DR7

Secondary

- » Systemic lupus erythematosus (most common cause of secondary APS)
- » Rheumatoid arthritis and Neoplasms
- » HIV, hepatitis A, hepatitis B, hepatitis C
- » Bacterial infections (e.g., syphilis, Lyme disease, tuberculosis)

DIAGNOSTIC APPROACH

History

- » Arterial or venous thrombosis
- » Recurrent miscarriages (≥ 1)

Serology for Antiphospholipid antibodies (APS)

1. **Most common** → **Lupus anticoagulant (LA):** Leads to a prolonged aPTT
 - **Mixing study:** The patient's plasma is mixed with normal plasma. If the prolonged aPTT is caused by a lack of clotting factors, the factors contained in the normal plasma will normalize the aPTT. In the presence of lupus anticoagulants, the aPTT will remain unchanged.
 - **Dilute Russell viper venom test:** Lupus anticoagulant interacts with Russell viper venom, which usually induces the formation of blood clots. As LA binds the venom, this effect is suppressed, resulting in a prolonged aPTT.
2. **Anticardiolipin antibodies (IgG and IgM):** Most commonly seen in patients with repetitive early pregnancy loss. Patients with APS often test **false positive for syphilis (positive VDRL or RPR)**, as the antigen used in syphilis tests is cardiolipin.
3. **Most Specific** → **Anti- β_2 -glycoprotein antibodies:** a group of antibodies that inactivate anticoagulant proteins (e.g., protein C, protein S, antithrombin-III) and activate platelets and vascular endothelium, thereby resulting in a hypercoagulable state

» **Blood tests:** CBC, LFTs, PT APTT & INR, heptoglobin, LDH (Thrombocytopenia, hemolysis, leukocytopenia)

Antiphospholipid syndrome (APS) usually manifests with recurring thrombotic events that may affect any organ.

» Venous

- Deep vein thrombosis
- Pulmonary embolism
- Livedo reticularis
- Ulceration (venous insufficiency)

» Arterial

- Stroke, transient ischemic attacks
- Occlusion of organ arteries (MI)
- Occlusion of distal extremity arteries (ischemia and gangrene)

» Capillaries: Splinter hemorrhages

» Pregnancy-related: Recurrent miscarriages and premature births



The key element of APS treatment is systemic anticoagulation.

Acute Management

- » **Low molecular weight heparin (LMWH) such as:**
Inj. Enoxaparin 40mg (Clexane) x SC
OR Unfractionated heparin x IV
Heparin/LMWH should be continued throughout pregnancy and stopped 7 days before onset of labour.
- » **In severe cases:** High-dose glucocorticoids, Plasmapheresis, and/or immunoglobulins

Secondary prophylaxis

- » **Low risk:** Low-dose aspirin → Tab. Ascard 75mg x OD
Should be started as soon as urine pregnancy test becomes +ve
Aspirin should be continued throughout pregnancy and stopped 7 days before onset of labour.
- » **High risk and no desire to become pregnant:** long-term treatment with oral warfarin
- » **Wish to have children:** LMWH PLUS Aspirin (prevention of miscarriage)

PUEPERAL SEPSIS



Definition: maternal sepsis that develops in the timeframe between birth and 6 weeks postpartum

Causative organism:

- » **Gram positive:** Strept. Pyogenes, Staph. Aureus (including MRSA), Strept. pneumoniae
- » **Gram negative:** E. coli, Klebsiella pneumonia
- » **Other:** Clostridium septicum, Morganella morganii

Risk Factors	Common Source Sites
» Obesity » Diabetes mellitus » Immunosuppression » Prolonged spontaneous rupture of membranes » Amniocentesis and cervical cerclage » Abnormal vaginal discharge, pelvic infection history » Vaginal trauma » Cesarean delivery » Retained products of conception	» Genital tract (e.g., endometritis) » Urinary tract (e.g., acute pyelonephritis) » Respiratory tract (e.g., severe pneumonia) » Breast (e.g., mastitis) and other skin/soft-tissue infections (e.g., episiotomy wound, IV site, indwelling catheters) » Group A beta-hemolytic streptococcal infection (<i>S. pyogenes</i>) acquisition or carriage » Gastrointestinal tract



C/C:

Clinical features:

Two or more of the following should be present

- » Fever
- » Pelvic pain
- » Abnormal vaginal discharge
- » Abnormal smell/foul odor discharge
- » Delay in uterine involution

DIAGNOSIS

- » Clinical features and pelvic examination
- » Send initial Lab test
- » Radiological test to find the source of infection (e.g., U/S pelvic, x-ray chest)

Complications

- » Septic shock
- » Clostridial myonecrosis
- » Death



- » **Stabilize ABCD&E**
- » Give supplemental oxygen
- » Maintain Intravenous line and draw initial laboratory studies
- » Continuous vitals monitoring and input/output record
 - » At least 2 sets of blood cultures
 - » Send Serum Lactate
 - » **Send additional labs:** CBC, LFTs, BUN, S/Electrolytes, Procalcitonin, CRP, and Serum calcium, PT/INR, ABGs and D-Dimer.
- » **Identify patients with septic shock:** Hypotension, elevated lactate
- » **Start Resuscitation measures.**
 - » Initial fluid resuscitation with 30 mL/kg of crystalloid.
 - » Add vasopressors if shock persists despite adequate fluid resuscitation
 - » Correct electrolyte imbalance
- » **Start Empiric Antibiotic Regimens for sepsis with unclear source. (Ideally within the first hour).**
 - » **Inj. Vancomycin 500mg to 1g** (Vancotic, Vinjec) x IV x TDS, diluted in 100ml 0.9% Normal saline and administer slowly over at least 60min at a rate of 10mg/min to prevent adverse infusion reactions (E.g., Red man syndrome).
Dosage: 15mg/kg IV every 8-12h
 - » **PLUS, one of the following:** should be dilute in 100ml 0.9% Normal saline
 - **Inj. Piperacillin/Tazobactam 4.5g** (Tazocin EF, Tanzo) x IV x TDS
 - **OR Inj. Meropenem 1g** (Meronem, Penro) x IV x TDS
 - **OR Inj. Ceftriaxone 2g** (Oxidil, Titan) x IV x OD
 - **OR Inj. Cefepime 2g** (Cefstar, Uceph) x IV x TDS
 - » **Inj. Metronidazole 500mg/100ml** (Flagyl, Metrozine) x IV x TDS
 - » **Inj. Esomeprazole 40mg** (Nexum, Eppo) x IV x OD
 - » **If Fever:** **Inj. Paracetamol 1g/100ml** (Provas, Bofalgan) x IV x TDS
 - » **Supportive care:** Normoglycemia, nutritional support and venous Thromboembolism (VTE) prophylaxis



POSTPARTUM ENDOMETRITIS

- ☞ **Definition:** inflammation of the endometrium, possibly also including the myometrium and parametrium
- ☞ **Causes:**
 - » Bacterial infection, often polymicrobial (involving multiple bacteria).
 - » Common bacteria include Streptococcus, Staphylococcus, and anaerobic bacteria.
- ☞ **Risk factors**
 - » Cesarean delivery (higher risk than vaginal delivery)
 - » Prolonged labor
 - » Prolonged rupture of membranes (more than 18 hours)
 - » Multiple vaginal/cervical examinations during labor
 - » Retained products of conception after delivery, miscarriage, or abortion
 - » Meconium in amniotic fluid
 - » Preexisting infections (e.g., bacterial vaginosis)
 - » Diabetes mellitus, Low socioeconomic status, Immunosuppression
- ☞ **Pathophysiology:** Lochia retention → ideal breeding ground for infection → postpartum endometritis / postpartum endomyometritis → postpartum sepsis

Clinical features

- » Fever (temperature 100.4°F)
- » Lower abdominal pain
- » Uterine tenderness
- » Foul-smelling lochia
- » Chills, malaise
- » Tachycardia

Diagnostic workup:

Primarily clinical; in some cases, the following tests can be used to confirm the diagnosis:

- » **CBC:** Elevated WBCs count
- » Gram stain or wet mount of vaginal discharge
- » **Blood and urine cultures**
- » **Endometrial Cultures:** Not routinely performed but may be considered in refractory cases.
- » **Ultrasound pelvic**

Complications: If untreated or inadequately treated, postpartum endometritis can lead to:

1. Pelvic abscess
2. Peritonitis
3. Sepsis
4. Infertility due to damage to the endometrium
5. Increased risk of future pregnancy complications



- ☞ Stabilize ABCD&E
- ☞ Establish Intravenous (IV) access
- ☞ IV fluid therapy and correct electrolyte imbalance

☞ Acceptable broad-spectrum antibiotic regimens include

- » **Inj. Ceftriaxone 2g** (Oxidil, Titan) x dilute in 100ml 0.9% NS x IV x OD
- » **PLUS, Inj. Metronidazole 500mg/100ml** (Flagyl) x IV x TDS
- OR **Inj. Ampicillin-Sulbactam 1.5 to 3g** (Ambac) x IV x TDS
- OR **Inj. Ertapenem 1g** (Invanz, Ernem) x BD

Alternative triple therapy with Inj. Ampicillin (2 g IV every 6 hours) + Inj. Gentamicin (1.5 mg/kg IV every 8 hours or 5 mg/kg once daily); and Inj. Clindamycin (900 mg IV every 8 hours) or Inj. Metronidazole 400 mg IV every 8 hours, until 24 to 48 hours afebrile.

- ☞ **Oral Step-Down Therapy:** After clinical improvement (typically 24-48 hours), patients can be switched to oral antibiotics to complete a total of 10-14 days of therapy.

☞ Supportive care

- » **Analgesia/Fever:** Inj. Paracetamol 1g/100ml (Provas) x IV x TDS
- » **Hydration:** Ensure adequate fluid intake and hydration.
- » **Monitoring:** Regular monitoring of vital signs and clinical status.

- ☞ Uterine curettage to remove retained products of conception.
- ☞ Hysterectomy in case of life-threatening complications or no response to conservative therapeutic measures.

EMERGENCY CONTRACEPTION "POSTCOITAL CONTRACEPTION"



- ✓ Use of a contraceptive within 5 days after unprotected intercourse to prevent pregnancy
- ✓ the sooner taken the more effective (75% to 80% effective if used within 72 hours of intercourse)
- ✓ Probably works by preventing or delaying ovulation; thus, it is not an abortifacient and will not work if a woman is already pregnant. Many options can be used as emergency contraceptive pills (dedicated products, progestin-only pills, combined oral contraceptive pills)
- ✓ **Most common form is 0.75mg of levonorgestrel given within 72 hrs of intercourse and repeated once 12 hrs later**
- ✓ **Alternatively: a single dose of 1.5 mg of Levonorgestrel** is probably equally effective with fewer side effects, and is available over the counter without age restrictions.
- ✓ Patient should expect usual menses within 21 days of treatment
- ✓ Main side effect of hormonal method is nausea and vomiting; consider simultaneous prescription of an antiemetic to take 1 hour before
- ✓ **The copper IUD can also be used as emergency contraception if inserted within 5 days of unprotected sex**
- ✓ **Contraindications:** Pregnancy, Undiagnosed pathologic genital bleeding
- ✓ Consider STI testing and HIV prevention after unprotected intercourse



C/C:

- » Cyclic Amenorrhea

Indications of EC

Recent unprotected intercourse
recent possible failure of a different mode of contraception (like condom rupture or missing/irregular pills).

For adolescents requesting emergency contraception with Ulipristal OR levonorgestrel, parental consent is not necessary

Efficacy trend: copper IUD > ulipristal > levonorgestrel



Non-hormonal methods

↳ Copper IUD

- » The most effective method of emergency contraception
- » must be inserted within 5-7 days of unprotected intercourse
- » Added benefit of long-term contraception
- » Requires brief, clinical procedure

Hormonal methods

- ✓ Most effective when taken within 3 days of intercourse (ulipristal acetate can be taken within 5 days (120 hours) of intercourse)
- ✓ Typically administered as a single dose or as two doses over one day
- ✓ Significantly less effective in patients who are obese or overweight

Types

- » **Levonorgestrel 0.75mg, 1.5mg**
- » **Antiprogesterin** (e.g., ulipristal acetate)
- » **Yuzpe regimen** (combination of ethinyl estradiol and levonorgestrel) as **Tab Famila 28F**

↳ **Tab. Ulipristal acetate 30mg (Ella-One)**

- » a progestin receptor modulator and delays ovulation
- » Must be taken within 120 hours after intercourse
- » Remains highly effective
- » The most effective oral Emergency Contraceptive
- » May require prescription.

↳ **OR Tab Levonorgestrel 0.75mg (ECP) or 1.5mg (Emkit-DS)**

- » Recommended to be taken within 72 hours after intercourse
- » still is effective up to 120 hours after intercourse
- » Efficacy is reduced
- » Available over-the-counter
- » Preferred over the estrogen-progestin regimen



OVERVIEW OF DIFFERENT TYPES OF HORMONAL CONTRACEPTIVES

Hormonal contraceptives involve the use of estrogen and progestin analogs to prevent pregnancy. The contraceptive effect is mediated by negative feedback at the hypothalamus, ultimately leading to reduced pituitary follicle-stimulating hormone (FSH) and luteinizing hormone (LH) secretion. Without an LH surge, ovulation does not occur. Progestin also makes implantation less likely, as it causes a thickening of cervical mucus, a decrease in tubal motility, and the inhibition of endometrial proliferation. Oral contraceptives (OCs) are the most common form of hormonal contraception, but other forms of hormone delivery, including patches, injections, and implants, also exist. In combination monophasic OCs, the dose of estrogen and progestin remains constant, while in combination multiphasic OCs it varies over the course of one cycle. The decreased total hormone doses of multiphasic OCs mitigate certain associated side effects and risks. These include bothersome symptoms such as breast tenderness, nausea, bloating, and breakthrough bleeding as well as medical emergencies such as venous thromboembolism. Because of the complications associated with hormonal contraceptives, their use is contraindicated in patients with certain medical conditions and histories, e.g., significant hypertension, ischemic heart disease, venous thromboembolism, and stroke.

Type	Description	Pregnancy rate in 1 st year with typical use (with perfect use)	Indications
<u>Oral contraceptive pill</u>			
Combined oral contraceptive (COC)	» Short-acting, reversible oral contraceptive containing estrogen and progestin » Monophasic or multiphasic	7% (< 1%)	» Contraception » Hyperandrogenism (e.g., acne, hirsutism) » Menstrual cycle disorders (e.g., menorrhagia, dysmenorrhea) » Symptom control in endometriosis, leiomyomas
Progestin-only contraceptive pills (minipill)	» Short-acting, reversible oral contraceptive containing low doses of norethindrone	7% (< 1%)	» Contraception for women in whom estrogen-containing contraceptives are contraindicated
Contraceptive patch	» Short-acting, reversible contraceptive transdermal patch that provides sustained low doses of estrogen and progestin	7% (< 1%)	» Patches are considered as effective as COC pills » Only require application to the skin once a week » Similar indications as for COC
Vaginal ring	» Short-acting, reversible flexible vaginal ring that contains ethinyl estradiol and etonogestrel	7% (0.3%)	» Similar indications as for COC
Injectable progestin	» Depot medroxyprogesterone acetate (DMPA): long-acting progestin-only contraceptive » Intramuscular (IM) or subcutaneous (SC) injection administered every 3 months	4% (0.2%)	» Long-term and reversible » For women who have contraindications for estrogen-containing contraceptive » A good option for women who may not remember to use short-acting contraceptives consistently.
Progestin intrauterine device	» Need to be replaced every 3 to 5 years (varies with type of device)	0.7% (0.5%)	» Long-term and reversible
Subdermal progestin implant	» The device (flexible plastic rod) is usually inserted subdermally in the upper arm and lasts 3 years	0.1%	

GYNAE & OBS DRUG BRANDS IN PAKISTAN



Levonorgestrel	» Tab. Emkit-DS (1.5mg)
	» Tab. Emkit 0.75mg
	» Tab. ECP 0.75mg
Estradiol Valerate 2 mg	» Tab. Progynova
Estradiol Dipropionate 5 mg	» Inj. Ovlogyn
Ethinyl estradiol 0.03 mg. + Levonorgestrel 0.15 mg + Ferrous Fumarate 75mg	» Tab. Famila-28F
	» Tab. Novodol
	» Tab. Nordette28
Desogestrel 0.15 + Ethinyl Estradiol 0.03	» Tab. Desofam
Ethinyl Estradiol 0.03mg + Drospirenone 3mg	» Tab. Yasmin
Ethinyl Estradiol 0.02mg + Drospirenone 3mg	» Tab. Yaz
Cyproterone Acetate	» Tab. Androcur 50mg
Cyproterone Acetate 2mg + Ethinyloestradiol 35mcg	» Tab. Diane-35
	» Tab. Cyprodiol
	» Tab. Acnot
	» Tab. Divestra
Estradiol Valerate 2mg + Norgestrel 0.5mg	» Tab. Progyluton
	» Tab. Estranor
Ethinylestradiol 0.02mg + Gestodine 0.075mg	» Tab. Dot-S
	» Tab. Meliane
Ethinylestradiol 35mcg + Norgestimate 250mcg	» Tab. Cilest
Orgametril 5mg	» Tab. Omatril
Testosterone	» Inj. Lyssa Depot 250mg/1ml
	» Inj. Testoviron Depot 250mg/1ml
	» Inj. Sustanon 250mg/1ml
	» Cap. Andrex 40mg
	» Testiva Gel 1% Sachet
Mesterolone	» Tab. Proviron 25mg
Dydrogesterone 10mg	» Tab. Duphaston 10mg
	» Tab. Dirogest 10mg
	» Tab. D-Gest 10mg
Estradiol 1mg + Dydrogesterone 5mg	» Tab. Femoston 1/5mg
Estradiol 1mg + Dydrogesterone 10mg	» Tab. Femoston 1/10mg
Estradiol 2mg + Dydrogesterone 10mg	» Tab. Femoston 2/10mg
Progesterone	» Cap. Progeffik 100mg & 200mg
	» Cap. Utrogestan 100mg & 200mg
	» Cap. U-Progest 100mg & 200mg
	» Cyclogest Pessary 200mg & 400mg
	» Cap. Utrogestan 100mg & 200mg
Hydroxyprogesterone 250mg	» Inj. Proluton Depot
	» Inj. Hydroxyprogesterone
Estradiol 5mg + Progesterone 250mg	» Inj. Gravibinan



Norethisterone 10mg + Ethinyl Estradiol 0.02mg	» Tab. Gynorit
Norethisterone 50mg/ml + Estradiol Valerate 5mg/ml	» Inj. Femiject-2month 1ml/ampule
» Provides effective contraception for 1 month	» Inj. Norifam 1ml/ampule
Norethisterone Oenanthate 200mg/ml	» Inj. Femiject-1month 1ml/ampule
» Provides effective contraception for 2 months	» Inj. Norigest 1ml/ampule
	» Inj. Novaject 1ml/ampule
Triphasic norgestimate/ethinyl estradiol	» Tab. Tri-sprintec
	» Tab. Tri-lo-mili
Triphasic norethindrone acetate/ethinyl estradiol/ferrous fumarate	» Tab. Mibelas 24-FE
	» Tab. Loestrin 24 -FE
Drospirenone/ethinyl estradiol/levomefolate	» Tab. Beyaz, Tab. Safyral
Norethisterone 5mg	» Tab. Primolut-N 5mg
	» Tab. Noregyn 5mg
	» Tab. Just-N 5mg
Methyl Oestrenolone 5mg + Methyl Ostradiol 0.3mg	» Tab. Mentona
	» Tab. Gynaecosid
Medroxyprogesterone acetate 150mg	» Inj. Depo-Provera 150mg/ml
» Provides effective contraception for 3 months	» Inj. Depoton 150mg/ml
	» Inj. Famila 150mg/ml
Intrauterine contraception	
» IUCD is one of the most effective, non-hormonal, long-term, reversible methods	
» This method does not require additional cost or visits to the provider once the IUCD is inserted.	
» Fertility returns immediately after removal of the IUCD.	
» IUCD can be used for emergency contraception within 5 days of unprotected intercourse.	
CU 200 Ag Silverline	» CU 200 Ag Silverline
» Protection up to 3 years.	
Cu375	» Protect 5 IUCD
» Safe and convenient method of birth spacing for upto 5yrs	» Heer - Cu 375 Sleek
Copper Y Cu 380	» Heer Copper Y Cu 380
» Protection up to 5 years	
» Cu Y acts by greatly reducing the likelihood of fertilization.	
» Cu Y involves inhibition of egg or sperm to fertilize egg.	
» Continuous Cu release in uterine cavity from the copper wire enhances the contraceptive effect of Copper Y.	
TCu380A	» Safeload 10 IUCD
» Highly safe and effective form of long-term reversible contraception for upto 10 years.	» Heer - T Cu 380A Safeload
	» Heer - T Cu 380A Plus
Levonorgestrel 75mg implant	» Jadelle sine inserter implant
Levonorgestrel 52mg T Shaped IUCD	» Mirena 52mg IUCD
Levonorgestrel 13.5mg; intrauterine system.	» Jydess 13.5 mg IUCD
	» Skyla 13.5 mg IUCD
Levonorgestrel 19.5mg; intrauterine system.	» Kyleena
Tibolone 2.5mg	» Tab. Livial
Use: Vasomotor symptoms associated with menopause.	» Tab. Tibol
	» Tab. Lobion-HRT



Oxytocin	» Inj. Syntomax 5 I.U. » Inj. Syntocinon 5 I.U.
Methylergometrin	» Inj. Methergin 0.2 mg » Tab. Methergin 0.125 mg
Ritodrine	» Inj. Yutopar 10mg/ml
Misoprostol	» Tab. Cytotec 200 mcg » Tab. S.T Mom 200 mcg » Tab. Breeky 200 mcg » Tab. Cytotol 200 mcg
Dinoprostone	» Tab. Prostin E2 3mg x Vaginally » Inj. Prostin F2 alpha 5mg/ml x IV » Tab. Preglan-E2 3 mg x Vaginally » Tab. Glandin-E2 3 mg x Vaginally » Glandin-E2 Vaginal Gel
Danazol	» Cap. Danocrine 100 mg, 200 mg » Cap. Danzol 100 mg, 200 mg
Gestrinone 2.5mg	» Cap. Dimetriose 2.5mg
Leuprolide acetate	» Inj. Lutrate Depot 3.75mg » Inj. Lutrate Depot 22.5mg
Goserelin Acetate	» Inj. Zoladex 3.6mg » Inj. Zoladex 10.8mg
Letrozole 2.5mg	» Tab. Femara 2.5mg » Tab. Lets 2.5mg » Tab. Retzole 2.5mg » Tab. Aromek 2.5mg
Anastrozole 1mg	» Tab. Arimidex 1mg » Tab. Femizet 1mg » Tab. Anastrozole Sandoz 1mg
Exemestane 25mg	» Tab. Aromasin 25mg
Tamoxifen 10mg	» Tab. Nolvadex 10mg
Raloxifene 60mg	» Tab. Evista 60mg
Human Menopausal Gonadotropin (Menotropin)	» Inj. IVF-M 75 I.U x IM/SC » Inj. Ferti-M 75 I.U x IM/SC » Inj. HMG Massone 75 I.U x IM/SC
Human Chorionic Gonadotropin (HCG)	» Inj. IVF-C 5000 I.U x IM/SC » Inj. Ferti-C 5000 I.U x IM/SC » Inj. Pregnyl 5000 I.U x IM/SC » Inj. Pubergen 5000 I.U x IM/SC
Urofollitropin (Purified FSH)	» Inj. Follimon 75 I.U x IM
Follitropin beta	» Inj. Puregon 100 I.U/0.5ml
Human Follicle Stimulating Hormone (Follitropin alpha)	» Inj. Follitrope 75 I.U & 150 I.U x SC » Inj. Gonal-F 75 I.U x SC
Clomiphene Citrate 50mg	» Tab. Clomid » Tab. Ovafin » Tab. Ovi-F



Conjugated Estrogens 0.3mg	» Tab. Premarin » Tab. Menorin » Premarin vaginal cream » Estromarin vaginal cream
Rho (D) Immune Globulin (Human) (ANTI-RH ₀ IG)	» Inj. RhoGAM 300 mcg (1500IU) » Inj. Rhophylac 300 mcg (1500IU) » Inj. Hyperrho 300 mcg (1500IU) » Inj. Immuno RHO 300 mcg (1500IU)
Clotrimazole vaginal use tablets/cream	» Canesten 10% vaginal cream » Canesten 100mg Vag tablets » Gynosporin 10% vaginal cream » Gynosporin 2% vaginal cream » Gynosporin 500mg Vag tablets
Miconazole	» Gyno-Daktarin vaginal cream » Myzovag vaginal cream
Isoconazole 1% vaginal cream	» Gyno-Travogen vaginal cream
Fenticonazole vaginal cream	» Lomexin 2% vaginal cream » Lomexin-T 1000mg ovule
Butoconazole nitrate 2% vaginal applicator	» Butacon 2% vaginal applicator » Femstat 2% vaginal applicator
Ciclopirox Olamine vaginal Ovule/suppositories	» Brumixol vaginal Ovule/suppositories
Metronidazole vaginal gel	» Metni-V cream » Metroaim V cream
Clindamycin vaginal cream	» Dalacin-V cream » Vagibact cream » Clinda-V cream
Nystatin + Neomycin + Polymyxin-B	» Polygynax Vaginal tablets
Metronidazole + Neomycin + Nystatin	» Tab. Neometin vaginal applicator
Tinidazole + Nystatin + Neomycin + Prednisolone	» Tergynan vaginal tablets
Lactobacillus casei, rhamnosus Döderleini	» Gynophilus Vaginal Cap
Lactobacillus rhamnosus, Lactobacillus delbrueckii, Streptococcus salivarius, Anti-Bacterial	» Fermalac Vaginal Capsule (Yogurt culture based - antibacterial)
Cynanchum Wilfordii, Phlomis Umbrosa, Angelica Gigas Indication: Estrogen Replacement Therapy (ERT)	» Tab. Formis 257.05mg
Myoinositol + D-Chiroinositol + Quatrefolic	» Tab. Femova
Myo-Inositol 2000 mg + Folic Acid 400 mcg	» Myofolic sachets » Inofolic sachets
Feminine Intimate Cleanser Vaginal wash (Enriched with lactic acid, Triclosan & Tea tree oil) Antifungal, antibacterial, control leukorrhea, PID	» Cran-V wash » VagiSaf Wash & VagiSaf Pro Wash » VegiWash » Famicyd
	»
	»
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U.S. FOOD AND DRUG ADMINISTRATION PREGNANCY DRUG CATEGORIES, 1979

DRUG CATEGORY	RISK DURING PREGNANCY
A	Controlled studies show no fetal risk in any trimester, and so the possibility of fetal harm is remote.
B	Animal studies show no fetal risk, but there are no controlled human studies. Or Animal studies have shown an adverse effect that was not confirmed in controlled human studies in women in the first trimester (and there is no evidence of risk in later trimesters).
C	Animal studies have shown adverse fetal effects (teratogenic or embryocidal), and No studies are available. Drugs should be used only, if the potential benefit justifies the potential fetal risk
D	Evidence of human fetal risk exists, but the benefits of use in pregnant women may be acceptable despite the risk.
X	Studies in animals or humans have shown fetal risk, or there is evidence of fetal risk based on human experience. The risk of use in pregnancy clearly outweighs any possible benefit. Drugs are contraindicated for use in women who are or may become pregnant.

DRUGS USED IN PREGNANCY WITH KNOWN ADVERSE EFFECTS IN HUMAN PREGNANCY

Antihypertensives (ACEIs) and Angiotensin receptor blockers (ARBs)	» Renal failure, oligohydramnios
Aminoglycosides	» Ototoxicity (Gentamicin class D , Black Box Warning)
Androgenic steroids	» Masculinize female fetus
Anticonvulsants (carbamazepine, hydantoins, sodium valproate)	» Dysmorphic syndrome, anomalies, neural tube defects
Antithyroid agents	» Fetal goiter
Aspirin (high doses)	» Bleeding, antepartum and postpartum
Cytotoxic agents (e.g., methotrexate)	» Multiple anomalies
Erythromycin estolate	» Maternal hepatotoxicity
Fluoroquinolones	» Fetal cartilage abnormality
Isotretinoin	» Hydrocephalus, deafness, anomalies
Lithium	» Congenital heart disease (Ebstein's anomaly)
NSAIDs (prolonged use after 32 wk.)	» Oligohydramnios, constriction of fetal ductus arteriosus
Streptomycin	» Fetal cranial nerve VIII damage
Sulfonamides	» Fetal hemolysis, neonatal kernicterus (near term)
Tetracyclines	» Fetal teeth and bone abnormalities
Trimethoprim, methotrexate	» Folate antagonist (first trimester)
Thalidomide	» Phocomelia
Warfarin	» Embryopathy – nasal hypoplasia, optic atrophy



SAFE MEDICINES IN PREGNENCY - CATEGORY 'B' DRUGS (CATEGORY 'C' ARE HIGHLIGHTED)
See section drug brands for brand names available in Pakistan

ANTI-EMETICS	☞ Metoclopramide (Metaclon) ☞ Doxylamine ☞ Dicyclomine ☞ Meclizine ☞ Ondansetron (Onset) ☞ Dimenhydrinate (Gravinate) ☞ Promethazine (Category-C)
DRUG FOR PEPTIC ULCER	☞ Famotidine ☞ Omeprazole (Risek) (Category-C) ☞ Pantoprazole (Zopent) ☞ Esomeprazole (Nexum) ☞ Sucralfate (Ulsanic)
ANTACIDS	☞ Aluminum hydroxide ☞ Magnesium hydroxide ☞ Calcium carbonate (Category-C) ☞ Simethicone (Category-C)
LAXATIVES	☞ Dietary fibre ☞ Isphaghol ☞ Lactulose ☞ Glycerine suppositories
ANALGESICS	☞ Paracetamol / Acetaminophen ☞ Non-steroidal anti-inflammatory drugs (NSAIDs): » Associated with oligohydramnios, premature closure of the fetal ductus arteriosus with subsequent persistent pulmonary hypertension of the newborn, fetal nephrotoxicity, and periventricular hemorrhage. » Use with caution 1st & 2nd Trimester; avoid in third trimester » Drugs: Ibuprofen, Naproxen, Ketorolac, Mefenamic, Diclofenac
ANTI-SPASMODIC	☞ Drotaverine ☞ Phloroglucinol
	☞ Penicillin group » Penicillin-G » Ampicillin (Penbritin) » Amoxicillin (Amoxil) » Cloxacillin » Piperacillin » Co-Amoxiclav (Augmentin) ☞ Cephalosporins (almost all are safe) » Cephalexin (Keflex)



ANTIBIOTICS	» Cephadrine (Velocef) » Cefaclor (Ceclor) » Cefuroxime (Zinacef) » Ceftriaxone (Rocephin) » Cefixime (Cefspan) ☞ Macrolides » Azithromycin (Azomax) » Erythromycin (Erythrocin) » Clarithromycin (Category-C) This drug should not be used during pregnancy unless there are no alternatives and the benefit outweighs the risk to the fetus. ☞ Clindamycin (Delacin-C) ☞ Vancomycin ☞ Nitrofurantoin (Fetus-Hemolytic anemia –Reported in some cases) ☞ Meropenem ☞ Aztreonam ☞ Fosfomycin ☞ Imipenem-cilastatin
ANTI-TUBERCULOUS	☞ Isoniazid ☞ Rifampicin ☞ Ethambutol ☞ Pyrazinamide
ANTI-ALLERGIC	☞ <u>Chlorpheniramine malate</u> ☞ <u>Diphenhydramine</u> ☞ <u>Loratidine (Softin)</u> ☞ <u>Cetirizine (Zyretic)</u> ☞ <u>Levocetirizine (Belair)</u> - Above Antihistamine are not recommended in the 1st trimester can lead to fatal defects - Consider Meclizine and Cyclizine in first trimester ☞ Saline nasal spray ☞ Oxymethazoline ☞ Xylometazoline
ANTI-AMOEBIAC	☞ Diloxanide furate ☞ Paramomycin ☞ Nitazoxanide ☞ Metronidazole (should be avoid in 1st Trimester) Use in First trimester: Fetus- Low birth weight babies, spontaneous abortions, and carcinogenic possibilities
ANTI-MALARIAL	☞ Chloroquine ☞ Mefloquine ☞ Quinine ☞ Proguanil - For first trimester
ANTHELMINTIC	☞ Piperazine ☞ Niclosamide



ANTI-FUNGAL	☞ Praziquantel
	☞ Clotrimazole (Category-C)
	☞ Miconazole (Category-C)
	☞ Nystatine
	☞ Terbinafine
	☞ Amphotericin-B
ANTI-VIRAL	☞ Butoconazole (Category-C)
	☞ Acyclovir
	☞ Famciclovir
ANTI-HYPERTENSIVE	☞ Valacyclovir
	☞ Methyldopa
	☞ Hydralazine
	☞ Metoprolol (Category-C)
	☞ Labetolol (Category-C)
	☞ Nifedipine (Category-C)
ANTI-DIABETIC	☞ Prazosin (Category-C)
	☞ Clonidine
HYPERTHYROIDISM	☞ Human insulin
	☞ Metformin
HYPOTHYROIDISM	☞ Propylthiouracil (First trimester)
	☞ Methimazole (2 nd trimester onward)
ANTI-EPILEPTIC	☞ Levothyroxine
ANTI-PSYCHOTIC	☞ Levetiracetam (Category-C)
	☞ Haloperidol
	☞ Trifluoperazine
ANTIDEPRESSANTS	☞ Prochlorperazine (Category-C)
	☞ Amitriptyline (Category-C)
	☞ Imipramine (Category-C)
	☞ Sertraline (Category-C)
ANTI-ASTHMATICUS	☞ Fluoxetine (Category-C)
	☞ Heparin (unfractionated and LMW)
	☞ Salbutamol
	☞ Ipratropium bromide
	☞ Beclomethasone
	☞ Budesonide
ANTI-DIARRHEAL	☞ Prednisone
	☞ Systemic steroids (Category-C)
OTHER DRUGS	☞ Imodium
	☞ Kaolin and pectin preparations (Kaopectate)
	☞ Folic Acid
	☞ Vitamin B6

Ref.1: <https://www.aafp.org/afp/2003/0615/p2517.html> (Over-the-Counter Medications in Pregnancy)

Ref.2: <https://www.just.edu.jo/DIC/Manuals/Evidence%20of%20drug%20safety%20in%20pregnancy.pdf>

Ref.3: https://jfmo.cchs.ua.edu/files/2013/09/Drugs_Pregnancy.pdf

World Health Organization (WHO) general cautions for drugs and breastfeeding

Guideline	Drugs
» BREASTFEEDING CONTRAINDICATED	» Anticancer drugs » Radioactive substances » Amphetamines » Ergotamines » Statins » Nitrofurantoin (for < 1 month old and for those with G6PD deficiency)
» AVOID UNLESS ABSOLUTELY NECESSARY	» Chloramphenicol » Tetracyclines » Fluoroquinolones
» MONITOR INFANT FOR DROWSINESS	» Selected psychiatric and anticonvulsant agents
» MONITOR INFANT FOR JAUNDICE	» Sulfonamides » Dapsone » Sulfadoxine/pyrimethamine (Fansidar) » Mefloquine
» MAY INHIBIT LACTATION (USE ALTERNATIVE DRUG)	» Estrogens » Thiazides diuretics

2015 U.S. Food and Drug Administration Pregnancy and Lactation Labeling Rule Required Information on Package Insert for Every Medication

IN BOTH PREGNANCY & LACTATION

- » **Risk summary:** What are the known risks in context with background risk?
 - » Risk statement based on human data
 - » Risk statement based on animal data
 - » Risk statement based on pharmacology
 - » Background risk information in general population
 - » Background risk information in disease population
- » **Clinical considerations:** What medical/disease factors should be considered?
 - » Disease-associated maternal and/or embryo/fetal risk
 - » Dose adjustments during pregnancy and the postpartum period
 - » Maternal adverse reactions
 - » Fetal/neonatal adverse reactions
 - » Labor or delivery
- » **Data:** Human and animal data and pregnancy drug registries that support the summary
- » **Human data:** Description includes study type, number, duration, exposure information & limitations.
- » **Animal data:** Description includes study type, species, animal doses and basis for the exposures, duration and timing, findings, presence of maternal toxicity, and limitations.

IN REPRODUCTIVE POTENTIAL

- » Contraception
- » Infertility
- » Pregnancy testing



FETAL RADIATION EFFECTS & CHARACTERISTICS

- For radiation imaging during pregnancy, weigh the risks of exposure and subsequent fetal adverse effects against the risk of incorrect maternal diagnosis.
- Major factor determining the degree of risk to the fetus is the quantity of ionizing radiation exposure during imaging.
- Fetal exposure to low-dose radiation, defined as <5 rads (<50 mGy)**
- DOES NOT increase the risk of fetal or infant death, mental defects, or growth retardation.
- More than 5 rads (>50 mGy) is considered the threshold for human teratogenesis.
- By using typical imaging parameters, it is unlikely that a single-phase CT scan would reach this dose level.
- The Fetus is most vulnerable to teratogenicity between 3 and 15 weeks of gestation at doses >10 rads (>100 mGy)
- The estimated radiation doses involved in procedures commonly used for ED diagnosis are listed below

TERATOGENIC RADIATION EFFECTS

GESTATIONAL AGE	EFFECT OF 5–10 RADS (50–100 mGy)	EFFECT OF >10 RADS (>100 mGy)
0 to 2 weeks	Probably none	Possible spontaneous abortion
3 to 8 weeks	Unknown; probably none detectable	Possible malformations with increasing dose
to 15 weeks	Unknown; probably none detectable	Possible mental development defects with increasing dose
>16 weeks	none	None detectable or none

RADIATION EXPOSURE TO THE UTERUS/FETUS

Procedure	Dosage in mGy
Threshold for human teratogenesis	100
Accepted as safe in pregnancy	50
Abdominal/pelvis CT	25–35
CT, kidney-ureter-bladder protocol (reduced radiation dose)	10
Lumbosacral spine series (three view)	1.6–3.5
Ventilation-perfusion scan (total)	2.1
Abdominal series (two view)	2
Lung perfusion scan with technetium	1.7
Normal background radiation over 9 months	1
Head CT	<0.5
Lung ventilation scan with xenon	0.4
Anteroposterior pelvis x-ray	0.4
Chest CT (10-mm slices, 10 slices), for standard or pulmonary embolism protocol	0.2
Cerebral angiography	0.1
Mammography—diagnostic for suspected breast cancers	0.07–0.2
Chest radiography (two view) with shielding of the maternal abdomen	<0.001
Cervical spine (two view)	<0.001

MRI IN PREGNANCY

The 2013 American College of Radiology guidance document on magnetic resonance safe practices states that MRI can be used in pregnant patients regardless of gestational age when the information gained is likely to alter treatment, when it cannot be obtained through other nonionizing means, and when MRI cannot be delayed until completion of the pregnancy. Noncontrast MRI (abdomen/appendicitis, pelvis/pelvic vein thrombosis) should be used unless contrast is deemed absolutely necessary given the recent concerns with gadolinium exposure to the fetus.

LACTATION AFTER IMAGING

The American College of Radiology and the American College of Obstetricians and Gynecologists advise that patients continue breastfeeding after administration of IV iodinated or gadolinium-based contrast agents. Both have low lipid solubility, and less than 1% of iodinated contrast agents and 0.04% of gadolinium-based contrast agents are excreted into breast milk.



THE NEWBORN INFANT

NEWBORN TERMINOLOGY

GENERAL

Infant:	A child under 1 year of age
Newborn (Neonate):	A child under 28 days of age
Perinatal period:	The period from the 22 nd week of gestation to the 7 th day after birth
Postpartum period:	First 6–8 weeks after birth
Live birth:	Postnatal presence of vital signs (e.g., respiration, pulse, umbilical cord pulse)

TIMING OF BIRTH

Term birth:	Umbrella term for live births between 37 and 42 weeks of gestation
» Early term infant:	Live birth between 37 0/7 weeks and 38 6/7 weeks of gestation
» Full term infant:	Live birth between 39 0/7 weeks and 40 6/7 weeks of gestation
» Late term infant:	Live birth between 41 0/7 weeks and 41 6/7 weeks of gestation
Preterm infant:	Live birth between 20 0/7 weeks and 36 6/7 weeks of Gestation
Postterm infant:	Live birth after The 42 nd week of Gestation

EVALUATION OF BIRTH WEIGHT

Appropriate-for-gestational-age infant (AGA):	Birth weight 10 th – 90 th Percentile for gestational age
Small-for-gestational-age infant (SGA):	Birth weight < 10 th Percentile for gestational age
Large-for-gestational-age infant (LGA):	Birth weight > 90 th Percentile for gestational age

Low birth weight

- » Birth weight < 2,500 g regardless of the gestational age
- » Occurs in early term infants and infants with intrauterine growth restriction
- » Associated with increased mortality, particularly due to sudden infant death syndrome
- » Very low birth weight: birth weight between 1,000–1,499 g regardless of the gestational age
- » Extremely low birth weight: birth weight < 1,000 g regardless of the gestational age

PREGNANCY LOSS

Miscarriage (spontaneous abortion) » Absence of vital signs » Pregnancy loss before the 20th week of gestation » Fetal weight less than 500g	Stillbirth (fetal death) » Absence of vital signs » Fetal death if pregnancy loss occurs during or after the 20th week of gestation. » Fetal weight more than 500g
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IMMEDIATE CARE OF THE NEWBORN

- » Wipe the newborn's mouth and nose to clear airway secretions, use suction only if necessary.
- » Dry and stimulate the newborn.
- » Provide warmth.
- » Skin-to-skin contact with mother and initiation of breastfeeding.
- » Clamp and cut the umbilical cord.
- » Apgar score assessment at 1 and 5 minutes after birth
- » Begin resuscitation if onset of respirations has not yet occurred within 30–60 seconds

APGAR SCORE

- » **Apgar score:** Appearance, Pulse, Grimace, Activity, Respirations
- » Used for standardized clinical assessment of newborns at 1 and 5 minutes after birth
 - » **Five components:** skin color, heart rate, reflex irritability to tactile stimulation, muscle tone, respiratory effort
 - » Each component is given 0–2 points, depending on the status of the newborn.
 - » The total Apgar score is the sum of all five components.
- » Assessing the need for and beginning neonatal resuscitation should be done independently of and before the Apgar score is determined
- » **Assessment of the Apgar score at 5 minutes:** infants with scores < 7 may require further intervention
 - » Reassuring: 7 – 10
 - » Moderately abnormal: 4 – 6
 - » Low: 0 – 3
- » In infants with a score below 7, the Apgar assessment is performed at 5-minute intervals for an additional 20 minute
- » Persistently low Apgar scores are associated with long-term neurologic sequelae.





CALCULATION OF THE APGAR SCORE

	0 Points	1 Point	2 Points
Appearance (skin color)	None	Pink trunk, blue extremities (acrocyanosis)	Pink body and extremities
Pulse (heart rate)	None	< 100 beats/min	≥ 100 beats/min
Grimace (reflex irritability upon tactile stimulation)	None	Grimace	Cry or active withdrawal
Activity (muscle tone, movement)	No movement, limp body	Some flexion	Active motion, flexion
Respirations	None	Weak cry, irregular/slow/weak breathing or gasping	Regular breathing, strong cry

The Apgar score is useful for evaluating the status of a newborn infant, but it should not be used to draw conclusions about individual neonatal morbidity or mortality and it should not be used as a long-term prognostic tool.

NEONATAL RESUSCITATION

- High-risk deliveries: should have a team of health care providers experienced in neonatal resuscitation on hand
 - » Maternal factors: very advanced maternal age or very young maternal age, diabetes or hypertension, substance abuse, previous fetal loss
 - » Fetal factors: prematurity, postmaturity, congenital anomalies, multiple gestations
 - » Complications of pregnancy and delivery: placental anomalies, oligohydramnios/polyhydramnios, transverse/breech delivery, chorioamnionitis, meconium-stained amniotic fluid, abnormal fetal heart rate, delivery with forceps/vacuum/cesarean
- Ventilatory resuscitation steps:
 - » Preductal pulse oximetry
 - » Dry the infant to place under the radiant heater.
 - » Place the infant with head in midline position neck with slight extension.
 - » Suction of mouth, oropharynx with a suction bulb.
 - » Assess the infant's condition: Respiratory effort (gasping or apnea or irregular breathing) and heart rate. Infants with regular breathing and heart rate >100 bpm need no further intervention; if cyanotic, provide O₂ supplementation.
 - » Most neonates can be effectively managed with a bag-mask ventilation (Positive pressure ventilation)
 - Indicated if there is gasping or apnea or irregular respiration OR an infant heart rate below 100 beat/minute
 - Intubation if pressure ventilation is ineffective or compressions are required
 - Restrictive use of supplementary oxygen guided by pulse oximetry
 - At birth, ventilation should be provided with room air for infant's ≥35 week's gestation.
 - Premature infants < 35 weeks gestation can receive FiO₂ 21–30% initially, titrated to SpO₂.
 - » Chest compressions: Indicated if heart rate is < 60 bpm despite adequate ventilation for 30 seconds. The sternum is compressed about one-third the diameter of the chest at regular rate of 90 compressions per minute while Ventilating (PPV), the infant at 30 breaths/min [3 chest compressions followed by 1 inflation (3:1)]. The HR is checked periodically and chest compression is discontinued when the HR is > 60 bpm. The thumbs are placed together over the lower third of the sternum. The palms encircle the torso and support the back. Preferably use the two thumb-encircling hands technique if two health care providers are present. Use the two finger technique if only one health care provider is present.
 - » IV Adrenalin (Epinephrine) at dose 0.1–0.3 mL/kg in 1:10,000 dilution is given IV or endotracheal, when there is persistent bradycardia. It may be repeated at every 5 minutes if heart rate < 60 bpm despite adequate ventilation and chest compressions for at least 30–60 seconds
 - » If there is no evidence of ROSC within 20 minutes, consider termination of resuscitation.



- Two thumb-encircling hands technique for chest compressions in neonates and infants
- Recommended technique if two healthcare providers are present:** Both hands are used to encircle the chest and chest compressions are performed with both thumbs placed on top of each other over the lower third of the sternum.
- This technique produces higher coronary artery perfusion pressure than the two-finger technique and more consistently results in effective compressions.

- Two-finger technique for chest compressions in neonates and infants
- Recommended technique if only one healthcare provider is present:** The chest is compressed using two fingers, which are placed on the lower half of the sternum (just below intermammary cleft).
- In comparison to the two-thumb-encircling hands technique, this allows for faster changes between compressions and delivering breaths when there is only one rescuer.



GENERAL AND SPECIFIC TREATMENT OF NEONATAL RESUSCITATION

General	specific
- Maintain ABCD&E approach. - Maintain thermo-neutral environment (Radiant warmer) - Monitor vitals, input/output record. - Correct electrolyte imbalance - IV fluid therapy – see below. - Correct hypoglycemia and metabolic acidosis ($\text{pH} < 7.2$)	CNS: IV Mannitol, IV Dexamethasone ($\uparrow$ ICP) and anti-epileptics for seizures. CVS: Inotropic support Acute Tubular Necrosis (ATN): IV fluid, dopamine & dialysis Hematological: FFPs, blood products (10 mL/kg) IV is given GIT: Consider Laparotomy (Mesenteric Ischaemia, NEC)

ASSESSMENT OF THE NEWBORN

Measurement and a detailed examination of the newborn should take place within the first 24 hours of life.

- Measurements:**
 - The normal range for newborn measurements at 40 weeks gestation is between the 10th and 90th percentiles.
 - Length:** the typical length is around 50 cm (48–53 cm)
 - Weight:** varies between 2.8 to 3.9 kg depending on gender (Boys: 2.9–3.9 kg, Girls: 2.8–3.8 kg)
 - The head circumference** is approximately 35 cm.
- Vital signs:** Check the newborn's respiratory rate (40 to 60 breaths per minute) and heart rate (120 to 160 beats per minute) to ensure they are within normal ranges.
- Evaluate serum bilirubin levels** (see "Neonatal jaundice")
- pH level:** ≥ 7.2 (slightly more acidic than adults)
- Ensure the newborn passes urine and meconium within specific timeframes after birth.**
 - First passage of urine within 24 hours of birth
 - First passage of meconium; (a black-green, tarry substance that forms the newborn's feces) within 48 hours after birth
- Feeding:** Encourage and provide guidance on breastfeeding, emphasizing its importance for newborn nutrition and bonding.
- Weight Changes After Birth:** Explain that it's normal for newborns to lose up to 7% of their birth weight in the first five days, with weight typically regained by 10 to 14 days old.
- Consequences of Intrauterine Estrogen Exposure:** Discuss the potential effects of intrauterine estrogen exposure, such as breast bud development and bloody mucoid vaginal discharge in newborn girls.
 - Breast bud development is normal in newborns, independent of sex.
 - Newborn girls may have bloody mucoid vaginal discharge.

EXTERNAL SIGNS OF MATURITY

- Skin color and texture:** A rosy skin color indicates good circulation and oxygenation. The texture of the skin is typically smooth and soft, reflecting the newborn's health.
- Body hair (Lanugo):** Lanugo, the fine, downy hair that covers the fetus in the womb, may be present on the newborn's body. It could be thinning or mostly absent, which is a normal part of the transition from intrauterine to extrauterine life.
- Eyes:** Newborns typically have open eyes shortly after birth, indicating alertness and awareness of their surroundings.
- Ears:** Well-formed pinna, the outer part of the ear made of cartilage, is a sign of maturity. When gently pulled or touched, the pinna should recoil or return to its original position instantly.
- Breast:** A clearly discernible areola around the nipple is a sign of breast development, which is normal in both male and female newborns due to maternal hormones.
- Testicles:** In male newborns, the testicles should be descended into the scrotum. This is an important sign of maturity and proper development of the male reproductive system.
- Labia:** In female newborns, the labia minora should be covered by the labia majora, indicating proper development of the external genitalia.
- Plantar creases:** The plantar creases, or the lines on the soles of the feet, should cover the entire surface. This is a sign of normal foot development and maturity.

PAEDIATRIC INTRAVENOUS (IV) FLUID PRESCRIBING

Indications for IV fluid

- Where possible, oral fluids (e.g. oral rehydration solution) via the oral or nasogastric route should be used. However, there are certain situations where the oral route is contraindicated or impractical. In these cases, it is necessary to determine the indication for fluids, type of fluid and volumes/infusion rate required.
- Three indications for IV fluids in infants and children: routine maintenance, replacement and resuscitation

1. Routine maintenance fluid:

- Maintenance fluid therapy is required if the current oral intake is not sufficient to remain hydrated.
- For example, if the patient is 'nil by mouth' for any significant period, full maintenance fluids will be required.
- Alternatively, if the patient can obtain some of their intake orally, but is not completely meeting their fluid requirements, they may be given a percentage of full maintenance fluids based on their intake.

2. Replacement fluids:

- Replacement fluid therapy is required if there is an existing fluid deficit, and the oral route is not possible or impractical.
- Examples of clinical situations where this may occur include: Prolonged poor oral intake, vomiting, diarrhoea, increased insensible losses (e.g. fever, excessive sweating), DKA, burn injuries.

3. Resuscitation fluids:

- Resuscitation is required if the patient is shocked.
- Types of shock with their underlying causes include:
 - Hypovolaemic shock: acute gastroenteritis, burns, diabetic ketoacidosis, heatstroke, haemorrhage.
 - Distributive shock: sepsis, anaphylaxis, neurological injury (neurogenic)
 - Cardiogenic shock: congenital heart disease, arrhythmia
 - Obstructive shock: cardiac tamponade, tension pneumothorax, congenital heart disease

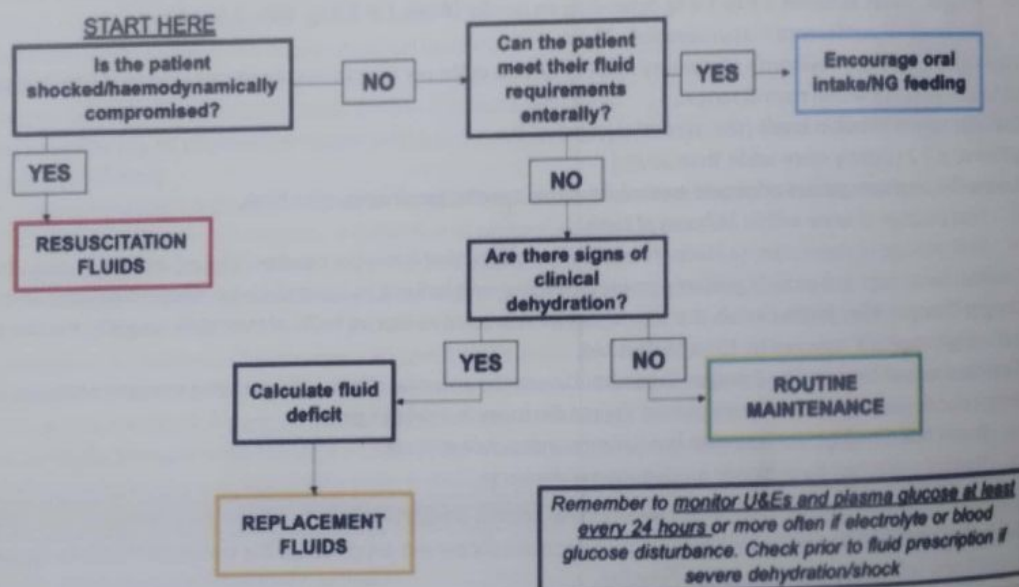


Figure: Algorithm for deciding the type of IV fluids by indication in infants and children.
Adapted from NICE algorithms for IV fluid therapy in children and young people in hospital.

[https://geekymedics.com/intravenous-iv-fluid-prescribing-in-paedics/#:~:text=For%20a%20child%20\(%3E28%20days,chloride%20%2B%205%25%20glucose\).](https://geekymedics.com/intravenous-iv-fluid-prescribing-in-paedics/#:~:text=For%20a%20child%20(%3E28%20days,chloride%20%2B%205%25%20glucose).)

INSENSIBLE WATER LOSS (IWL) IN NEWBORN

- A newborn undergoes rapid changes in both extracellular and intracellular body fluid compartments and composition during the first week of life
- Insensible water loss occurs via the skin and mucous membrane (2/3) and respiratory tract (1/3).
- An important variable influencing insensible water loss (IWL) is the maturity of neonate skin, with greater insensible water loss (IWL) in preterm babies resulting from evaporation through the immature epithelial layer.



Serial weight charting:

- » Weight need to be checked at least once per day upto a minimum of 10 grams.
- » Term babies lose 1-2% of their birth weight daily with a cumulative loss of 5-10% in the first week of life.
- » Preterm babies lose 2-3% of their birth weight daily a cumulative loss of 15-20% during the same period.
- » If the daily weight loss is either <1% or >3%, it is abnormal (Ref: Neonatology Practice Made Easy)

INSENSIBLE WATER LOSS (IWL) ACCORDING TO BIRTH WEIGHT

Birth weight in grams	IWL ml/kg/day
< 750g babies	100 – 200
750g – 1000g	60 – 70
1001g – 1250g	50 – 60
1251g – 1500g	30 – 40
1501g – 2000g	20 – 30
>2000g	15 – 20

Factors affecting insensible water loss

Increase IWL	Decrease IWL
» Low maturity » Low relative environmental humidity » Hyperthermia (↑ Temperature 30%) » Skin defects (omphalocele, gastroschisis) » Non-humidified inhaled oxygen » Phototherapy and use of radiant warmer	» Higher maturity » Increasing postnatal age » High environmental relative humidity » High ventilator relative humidity » Double wall incubator » Topical skin agent: olive oil, paraffin

Daily maintenance fluid

Daily maintenance fluid requirement in >1.0 kg babies

Age/Days	Birth weight		Fluid type
	1 – 1.5 kg	> 1.5 kg	
1	80 ml/kg/day	60 ml/kg/day	10% Dextrose
2	100 ml/kg/day	80 ml/kg/day	
3	120 ml/kg/day	100 ml/kg/day	10% Dextrose + 0.18% saline
4 to 28 day	120-150 ml/kg/day	100-150 ml/kg/day	

Daily maintenance fluid requirement in >1.0 kg babies

Age/Days	Birth weight		Fluid type
	<800 gram	> 800 gram	
1	100 – 120 ml/kg/day	80 – 100 ml/kg/day	5 – 7.5% Dextrose
2	120 – 140 ml/kg/day	100 – 120 ml/kg/day	
3 to 28 day	140 – 160 ml/kg/day	130 – 160 ml/kg/day	10% Dextrose + 0.18% saline

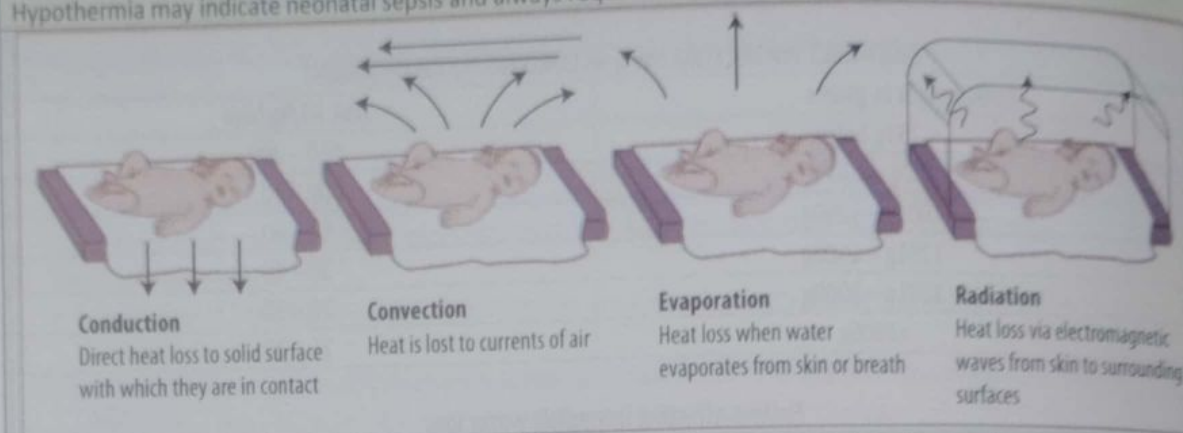
Children (28 days to 18 years of age)

Holliday-Segar formula (4,2,1 rule):

- » 4 mL/kg/hour for the first 10 kg
- » + 2 mL/kg/hour for the next 10 kg
- » + 1 mL/kg/hour for the remaining weight

NEONATAL HYPOTHERMIA

Pathophysiology: Neonates have thin skin, little adipose tissue and a large body surface area comparative to their body weight; they are therefore very susceptible to heat loss and consequent hypothermia. Hypothermia may indicate neonatal sepsis and always requires assessment of the baby.



Physiology or types of neonatal heat loss (image source: obgynkey.com)

Epidemiology

- » Hypothermia can develop quickly in preterm and unwell neonates.
- » Hypothermia leads to a significant increase in morbidity and mortality in the newborn period and should be aggressively avoided

Risk factors.

- » Prematurity
- » Systemic illness
- » Birth $\leq 2^{\text{nd}}$ centile
OR clinically wasted
- » Babies of diabetic mother



☞ Babies lose heat through four different ways: conduction, convection, evaporation, and radiation.

☞ This should be combatted by:

- » Warm mattress/skin to skin with Mum (conduction)
- » Keeping room temperature warm and avoiding draughts (convection)
- » Wrapping baby, including hat and socks (evaporation)
- » Using incubator as radiant heat source (radiation)

Mechanisms of heat loss and prevention

Mechanism	Example	Prevention
Conduction	Heat loss into a cold surface directly under the baby. Heat loss into cold (ER) equipment	Warm the Resuscitaire towels prior to delivery, Discard wet towels, Prewarm the incubator, Do not place cold radiography plates directly in contact with the baby's skin, Warm hands and stethoscope before examining the baby, Kangaroo care – placing baby directly against a parent's chest
Convection	Heat loss directly into currents of air	Place newborn preterm infants in a plastic bag or wrap Do not place the baby near open windows or air vents Use closed incubators rather than open platforms if possible Close the doors to the nursery Close the incubator doors after a procedure
Evaporation	Heat lost when water evaporates from the baby's skin as water vapour Evaporation of water (and therefore heat loss) from the lungs during expiration	Place newborn preterm infants in a plastic bag or wrap, Dry newborn term infants immediately with warm, dry towels, Humidify the environment (e.g. the incubator) Humidity and warm ventilation gases, Cover open tissue (e.g. skin burns or gastroschisis)
Radiation	Heat loss (via infrared radiation) to another surface, which is not in contact with the baby or down a concentration gradient via surrounding air	Maintain the whole nursery at a warm temperature, Use double-walled incubators, Do not come between the baby and an overhead heater, Cover the baby's head (large surface area) with a hat

VITAMIN-K DEFICIENCY BLEEDING (VKDB) OF THE NEWBORN

CLINICAL FEATURES

- » Early onset: within 24 hours after birth; intracranial bleeding common
- » Classic: within 4 weeks after birth; intracranial bleeding rare
- » Late onset: between 2–8 months after birth; intracranial bleeding common.

DIAGNOSTIC WORKUP

- » History and physical examination
- » Complete blood count (CBC)
- » Reticulocytes count
- » Coagulation profile:
 - » Prothrombin (PT): ↑
 - » Activated partial thromboplastin time (aPTT): ↑ or normal
 - » Bleeding time: Normal
 - » Factors II, VII, IX, and X: ↓
- » Von Willebrand panels are done where family history is positive.

ETIOLOGY

- » **Exclusive breastfeeding:** Low vitamin-K levels in breast milk
- » Low liver storage capacity and Poor placental passage of vitamin-K
- » **Abnormality in clotting:** DIC, due to infection, anoxia, shock and NEC
- » **Medications:** received by mother during pregnancy—phenytoin, warfarin, rifampicin, salicylates (affect vitamin K function)
- » Underdeveloped intestinal flora (which produces vitamin K), e.g., due to premature birth and Chronic diarrhea of the newborn
- » Platelet dysfunction & Inherited coagulation defect (hemophilia, VWD)
- » Long-term antibiotic treatment in newborns
- » Cholestatic diseases (biliary atresia), liver dysfunction



TREATMENT OF VKDB OF THE NEW BORN

- » **Inj. Vitamin-K₁** (Phytonadione) at dose 1mg IV slow or IM, may be repeated weekly.
- » Fresh frozen plasma (FFP) at dose 10 mL/kg IV, may have to be repeated. FFP replaces clotting factors immediately.
- » Consider platelets and whole blood transfusion if indicated
- » Clotting factor concentrates may be given when there is a known deficiency (e.g. factor VIII, IX or VMD), to stop bleeding
- » Treatment of specific problems, e.g. sepsis, DIC

NEONATAL POLYCYTHEMIA

Definition: Neonatal polycythemia (erythrocythemia) is defined as abnormal elevation of the circulating red blood cell mass. Venous hematocrit (HCT) greatly exceeding normal values for gestational and postnatal age.

Neonatal polycythemia C/C:

- » Asymptomatic
- » Respiratory distress
- » cyanosis, apnea
- » Poor feeding
- » vomiting
- » Hypoglycemia
- » Plethora (Reddish complexion)
- » Lethargy and irritability
- » Tremors or seizures
- » Feeding difficulties
- » Hypoglycemia
- » hypocalcemia

Diagnostic workup:

- » CBC: Hemoglobin (Hb) > 22 g/dL and Haematocrit (Hct) > 65%
- » Total serum bilirubin
- » Serum glucose
- » Serum calcium
- » Serum urea and creatinine
- » Serum electrolytes

Epidemiology: 1–5% of newborns

Risk factors

- » Small for gestational age (SGA)
- » Large for gestational age (LGA)
- » Twin-to-twin transfusion syndrome (recipient)
- » Placental abruption, perinatal asphyxia and pre-eclampsia.
- » Neonatal Hypothyroidism & IUGR
- » Maternal tobacco/alcohol use
- » Perinatal asphyxia
- » Infants of diabetic mothers
- » Chromosomal abnormalities
- » Delayed umbilical cord clamping
- » **Drugs:** propranolol, oxytocin administration

Complications

- » Hypoglycemia
- » Hyperbilirubinemia
- » Necrotizing enterocolitis (NEC)



- » Monitoring
- » IV hydration
- » **Correction of electrolyte imbalance:** Hypocalcemia, Hypoglycemia
- » **Correct underlying cause:** E.g., Apnea, seizures, NEC.
- » **Partial exchange transfusion:** a procedure in which part of the blood is replaced with an isotonic fluid to lower the hematocrit
 - » Indicated in asymptomatic patients with high hematocrit (> 75%) or symptomatic patients with hematocrit (Hct) > 65%
 - » Increased risk of Necrotizing enterocolitis (NEC)



NEONATAL HYPOCALCAEMIA

CAUSES OF NEONATAL HYPOCALCAEMIA

Early onset < 3 days of life	Late onset > 3 days of life
Maternal causes: » Maternal drugs intake of ▪ Phenobarbitone ▪ Phenytoin sodium Neonatal causes: » Prematurity (<32 weeks) » Intrauterine growth restriction (IUGR) » Infants of diabetic mother » Birth asphyxia » Hypoxic ischaemic encephalopathy » Hypomagnesaemia » DiGeorge syndrome	Maternal causes: » Hyperparathyroidism » Vitamin-D Deficiency » Hypercalcaemia Neonatal causes: » Hyperphosphataemia » Hypomagnesaemia » Vitamin-D Deficiency » Transient Hypoparathyroidism » DiGeorge & Kenny-Caffey syndrome » Phototherapy, Exchange transfusion, Alkalosis & bicarbonate therapy » Use of Furosemide, and steroids » Sepsis and septic shock

▲ Neonatal Hypocalcaemia

c/c

Recognition and Assessment

- » Term or preterm infants: Birth weight ≥ 1500 g, total serum calcium < 2 mmol/L or ionised fraction < 1.1 mmol/L
- » Preterm infant: Birth weight < 1500 g, total serum calcium < 1.75 mmol/L or ionised fraction < 1 mmol/L

Symptoms and signs

- » Early onset occurs in first <3 days of life and is usually asymptomatic.
- » Late onset develops after first >3 days of life and typically occurs at the end of the first week
- » Most infants are asymptomatic and identified on screening
- » Characteristic sign is increased neuromuscular irritability including:
 - Jitteriness, tetany and irritability
 - Generalised/focal seizures
 - Non-specific symptoms e.g.:
 - Poor feeding
 - Lethargy
 - Apnoea
 - Prolonged QT interval on ECG
 - Abdominal distension
- » Rare presentations:
 - Stridor
 - Bronchospasm
 - Pylorospasm

Diagnostic workup:

Early onset < 3 days of life

- » Serum calcium
- » Serum Phosphate
- » Serum Magnesium
- » Serum alkaline phosphatase
- » Persistent hypocalcaemia or severe hypocalcaemia despite adequate calcium therapy:
 - 25-hydroxyvitamin-D level
 - BUN and creatinine
 - Serum parathyroid hormone
 - Urinary calcium: creatinine ratio

Mother tests

- » Serum calcium
- » Serum Phosphate
- » Serum alkaline phosphatase
- » 25-hydroxyvitamin-D level
- » ECG: Prolonged QT interval

Rx

Asymptomatic but high-risk infants

- » Most infants with early onset hypocalcaemia recover with nutritional support, so early feeding provides adequate calcium.
- » Infants requiring IV fluid: add calcium gluconate 10% 2mL/kg/day (=0.46 mmol/kg/day) to IV fluid and give as continuous infusion
- » Infant tolerating oral feeds: Give elemental calcium 50 to 60mg/kg/day orally three divided doses.

Symptomatic hypocalcaemia

- » Give inj. Calcium gluconate 10% x 0.5–2mL/kg IV STAT, diluted with Dextrose water 5% or Normal saline 0.9%. (1:1 dilution) over 15–20 min.
- » Followed by maintenance dose: inj. Calcium gluconate 10% x 1–2mL/kg IV stat, diluted with Dextrose water 5% or Normal saline 0.9%. (1:1 dilution) over 15–20 minute x every 6 hourly or 4–8mL/kg/day as continues IV infusion for 48 hours with continuous cardiac monitoring.
 - » Check serum calcium level after 48 hours → Hypocalcaemia → Continues above same treatment for one more day.
 - » Serum calcium level normal → Stable baby or following acute treatment consider oral calcium at dosage 50–60mg/kg/day in three divided doses for 2–3 days.
 - » If prolonged hypocalcaemia → Continue oral calcium supplement if infant oral feed tolerated well, otherwise continue IV infusion and investigate further to determine the etiology (see investigation)
- » If hypomagnesaemia: Inj. magnesium sulphate at dosage 100mg/kg or 0.2mL/kg x IV/IM 12-hourly for 2–3 divided doses
- » Vitamin-D deficiency: Give cholecalciferol 1000–2000 IU x daily and adjust dose according to response.
- » Cholecalciferol Brands:
 - » Infant Drops: Miura-D 400IU or D-max 400IU, or All-D 400IU x PO
 - » Injection: Miura-D 5mg, D-All 5mg, Indrop-D 5 mg x IM/PO
- » Hyperphosphataemia/increased phosphate load
 - » Stop cow's milk, Breast feeding is preferable, if not available, use infant formula milk with low phosphate 60/40 (Similac PM 60/40 milk) and oral calcium (Syp. Calcium-P 210mg/5ml)
 - » Consider high calcium, low phosphate diet
 - » Oral calcium and phosphate normalise in 3–5 days. Stop calcium after 1 week and switch to normal formula in 2–4 weeks

NEONATAL HYPOGLYCAEMIA

Pathophysiology: Hypoglycaemia (Blood sugar level <2.6 mmol/L or <47 mg/dL) is a common problem in newborns.

Warning: Four are the risk factor and causes of babies hypoglycemia

- 1. Glucose production: Sepsis, Hypothermia (cold stress), perinatal asphyxia, increased work of breathing
- 2. Glucose demands: Babies of diabetic mother, Beckwith-Wiedemann syndrome, Islet cell hyperplasia, erythroblastosis fetalis
- 3. Hypoparathyroidism: Adrenal insufficiency, panhypopituitarism, hypothyroidism

- 4. Risk factors
 - Prematurity
 - Systemic illness
 - Inadequate growth restriction
 - Inadequate growth (table) or clinically wasted
 - With 32nd centile mother
 - Babies of diabetic mother
 - Babies of mother taking beta blockers in third trimester
 - Babies of mother at time of delivery

Table: 2nd centile weights for boys and girls by week of gestation

Gestational Age (week)	Boys Weight (kg)	Girls Weight (kg)
37 weeks	2.10	2.00
38 weeks	2.30	2.20
39 weeks	2.50	2.45
40 weeks	2.65	2.60
41 weeks	2.80	2.75
42 weeks	2.90	2.85

Clinical features

CLINICAL SIGNS SUGGESTIVE OF HYPOGLYCAEMIA are an

expression of 21 of the following clinical signs/diagnoses: is an

expression to measure blood glucose:

admission to measure blood glucose:

- Perinatal acidosis (cord arterial or baby pH <7.1 and base deficit >10)
- Hypothermia ($<36.5^{\circ}\text{C}$) not attributable to environmental
- Icterus
- Suspected confirmed early neonatal sepsis
- Cyanosis
- Apnoea
- Altered level of consciousness
- Seizures
- Hypotonia
- Lethargy
- High pitched cry/abnormal cry
- Abnormal feeding behaviour (not waking for feeds, not sucking effectively), appearing unsettled, demanding very frequent feeds, especially after a period of feeding well may be indicative of hypoglycaemia
- Tremors (excessive repetitive movements of ≥ 1 limb which are unprovoked and not in response to stimulus) is common and is not by itself an indication to measure blood glucose.

Diagnostic workup

- Check bed side blood sugars and temperature regularly in NICU settings. If identified investigate driving cause.
- Symptomatic or severe (<1.5 mmol/L) hypoglycaemia in a newborn should prompt a 'hypo screen'. This looks for endocrine and metabolic and other causes.
- **Indications for further investigations**
 - » Persistent hypoglycaemia (>2 measurements <2.0 mmol/L within the first 48 hour of life)
 - » Severe hypoglycaemia (<1.0 mmol/L) at any time
 - » Signs of acute neurological dysfunction and blood glucose <2.5 mmol/L at any time

INVESTIGATIONS TO RULE OUT UNDERLYING CAUSE

- Blood test include:** glucose, insulin, cortisol, growth hormone, fatty acids, ketone bodies, carnitine, acylcarnitine profile, amino acids, ammonia, lactate and
- Urine test:** Urine ketones, urine organic acids and Review need to screen for/treat sepsis.

Further investigations based on results of initial screen and following specialist advice.

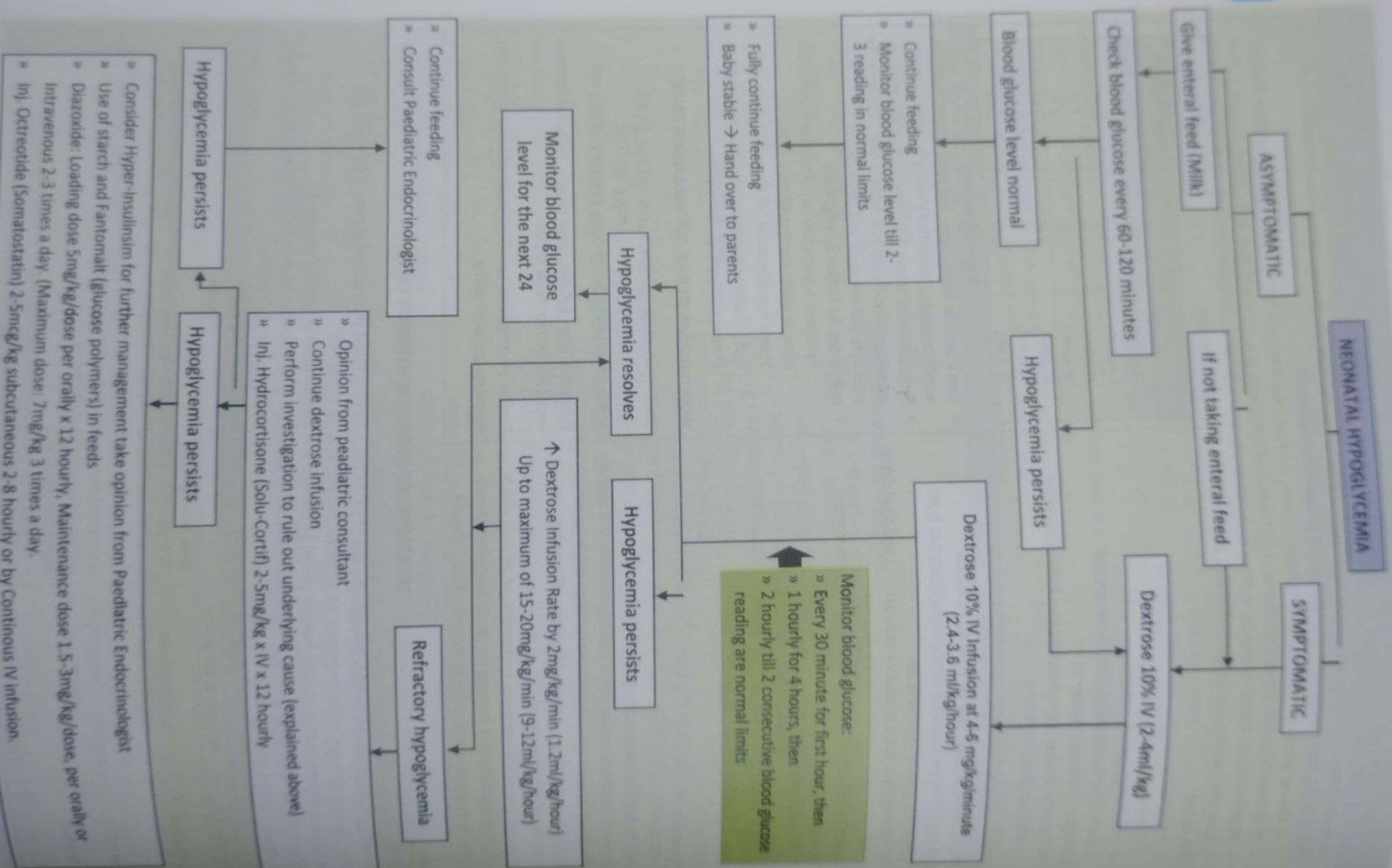
TREATMENT OF NEONATAL HYPOGLYCAEMIA

Treatment guidelines (shown in table below): The aim of treatment is to keep blood glucose level above >2.8 mmol/L (50 mg/dL) in the first 48 hours of life and above >3.3 mmol/L (60 mg/dL) after this period.

- In hyperosmolar states, glucose boluses should be avoided and a higher glucose infusion rate used.
- After initial correction with a bolus of 10% dextrose in water (D10W; 2mL/kg), glucose infusion should be increased gradually to needed from a starting rate of 4-6 mg/kg/minute, and weaned slowly when normoglycemic.

Table: Hypoglycemia - suggested therapeutic regimens

Testing Test	Presence of Symptoms	Action
≥ 40 mg/dL	No symptoms of hypoglycemia	Draw blood glucose » If the infant is alert and vigorous, feed; follow with frequent glucose monitoring. » If the infant continues to have blood glucose <40 mg/dL or is unable to feed, provide IV Glucose at 4-6mg/ kg/minute (Dextrose 10% at 2.4 to 3.6 mL/kg/hour).
<40 mg/dL	Symptoms of hypoglycemia present	Draw blood glucose: Provide bolus of Dextrose 10% (2 mL/kg) followed by an infusion of 6 mg/kg/minute (3.6 mL/kg/hour).
<30 mg/dL	With or without symptoms of hypoglycemia	Draw blood glucose: » Provide bolus of Dextrose 10% followed by an IV infusion of 6 mg/kg/min. » If IV access cannot be obtained immediately, an umbilical vein line should be used.



NEONATAL RESPIRATORY DISTRESS SYNDROME (NRDS)



Definition: Neonatal respiratory distress syndrome (NRDS), or surfactant deficiency disorder, is a lung disorder in infants that is caused by a deficiency of pulmonary surfactant. It is most common in preterm infants, with the incidence and severity decreasing with gestational age. Surfactant deficiency causes the alveoli to collapse, resulting in impaired blood gas exchange.

Clinical features

- » History of premature birth
- » Onset of symptoms: usually immediately after birth (<4 hours) but can occur within 48–72 hours postpartum
- » Distressed and unwell infant.
- » Poor feeding.
- » Signs of increased breathing effort
 - Tachypnoea (> 60 breaths/minute).
 - Hypoxia.
 - Nasal flaring; and moderate to severe subcostal/intercostal and jugular retractions
- » Typical expiratory “grunting” (in an attempt to increase airway pressure and open collapsed alveoli).
- » Auscultation: decreased breath sounds
- » Cyanosis due to pulmonary hypoxic vasoconstriction.

Diagnostic workup

- » **Clinical:** Integration of typical physical examination findings and patient history
- » **Chest x-ray**
 - Interstitial edema: especially perihilar, given the appearance of bilateral perihilar streaking
 - Diffuse, fine, reticulogranular (ground-glass) densities with low lung volumes and air bronchograms
- » **Blood gas analysis (ABGs)**
 - Hypoxia with respiratory acidosis; can lead to increased lactate levels
 - Evaluate for partial respiratory failure or global respiratory failure
- » **Amniocentesis for prenatal testing of NRDS:** screening for markers of fetal lung immaturity → Lecithin-sphingomyelin ratio < 1.5 (≥ 2 is considered mature)

Rx

- » The aim of treatment is to create a homeostatic environment for the neonate to produce their own surfactant and thus self-ventilate. This can only happen in the presence of normal pH, temperature and sufficient oxygenation.
- » The baby should be placed in neonatal intensive care unit (NICU) and nursed in a warm incubator with high humidity (neutral thermal condition). Air passage is cleaned periodically through endotracheal suction.
- 1. **Ventilation:** Continuous positive airway pressure (CPAP) and mechanical ventilation to give sufficient pressure to open the airways and prevent further lung collapse.
 - » Nasal CPAP with a PEEP at 5–8 cm of water is indicated.
 - » If respiratory insufficiency persists, start intubation with mechanical ventilation and O₂ inhalation.
 - » **Supplement O₂:** Adjust inspired oxygen to maintain SpO₂.
- 2. **Endotracheal surfactant therapy:** Endotracheal administration of artificial surfactant within 2 hours postpartum and decrease alveolar surface tension.
 - » Natural surfactant, **poractant alfa** (Curosurf®) 200 mg/kg (2.5 mL/kg) round to the nearest whole vial
- 3. **Supportive measures:**
 - » IV fluid replacement & correction of electrolytes imbalance
 - » Correct hypothermia, acidemia, anemia and hypoglycaemia.
 - » **Consider antibiotics** to prevent secondary bacterial infection
- 4. **Antenatal maternal administration of corticosteroids**
 - » If possible, give antenatal corticosteroids to the mother prior to delivery in at-risk pregnancies.

INCIDENCE OF RESPIRATORY DISTRESS SYNDROME BY GESTATIONAL AGE & ANTENATAL STEROID ADMINISTRATION

Gestational Age (week)	Antenatal Steroids Administered	Antenatal Steroids Not Administered
<30 weeks	35%	60%
30–34 weeks	10%	25%
34–36 weeks	1.4%; 5.5%	2.3%; 6.4%
>37 weeks	2.6%	5.4%

» Neonates with severe respiratory distress syndrome.

» **Note:** The use of antenatal corticosteroids in >34 weeks gestational age is controversial due to inconsistent data regarding efficacy and limited data regarding long-term effects.

- » Antenatal maternal administration of steroids >24 hours and <7 days prior to delivery, has been shown to decrease neonatal morbidity and mortality.
- » **Inj. Betamethasone 4mg/1ml** (Betnesol) x 12mg x IM x OD for 2 days OR **Inj. Dexamethasone 4mg/1ml** (Decadron) x 6mg x IM x BD for 2 days.

SURFACTANT REPLACEMENT THERAPY (GUIDELINES)

- Early administration of natural surfactant decreases the risk of acute pulmonary injury and neonatal mortality. Early CPAP, and selective administration of surfactant is preferable to routine intubation and prophylactic surfactant.
- Natural surfactant preparations are superior to protein-free synthetic preparations containing only phospholipids for reducing mortality and air leaks.
- Poractant alfa (Curosurf) at dose 2.5 mL/kg (200 mg/kg) shows survival advantage compared to Beractant (Surfanta) or Poractant Alfa in a dose 4 mL/kg (100 mg/kg).
- Multiple rescue doses result in greater improvements in oxygenation and ventilatory requirements, a decreased risk of pneumothorax and a trend toward improved survival.
- Use of Intubate-Surfactant-Extubate (INSURE) to CPAP or LISA (Less Invasive Surfactant Administration) or Minimally Invasive Surfactant Treatment (MIST) techniques for early surfactant administration reduce the need for ventilation and improve survival.

INDICATIONS: Prophylaxis (administration ≤ 15 min of birth)

Babies born <28 weeks' gestation

- Routine intubation of these babies solely for the purpose of administration of surfactant is not necessary, and a policy of early CPAP with selective surfactant administration is preferred.
- If requiring intubation for respiratory support during resuscitation or if mother has not had antenatal steroids, give surfactant as prophylaxis.
- Otherwise, institute early CPAP and administer surfactant selectively as per Early rescue treatment.

Early rescue treatment

- Preterm babies who require invasive ventilation for stabilisation should be given surfactant.

Babies born ≤ 33 weeks' gestation who are not ventilated

- If $\text{FiO}_2 > 0.30$, give surfactant using minimally/less invasive technique or after invasive ventilation.

Other babies that can be considered for surfactant therapy (after discussion with consultant)

- Ventilated babies with meconium aspiration syndrome (may need repeat dose after 6–8 hr).
- Term babies with pneumonia and less compliant lungs.

EQUIPMENT

- Natural surfactant, poractant alfa (Curosurf®) 200 mg/kg (2.5 mL/kg) round to the nearest whole vial (prophylaxis and rescue doses can differ).
- Sterile gloves.
- TrachCare Mac catheter (do not cut NGT) or specific surfactant administration set.

PROCEDURE**Preparation**

- Calculate dose of surfactant required and warm to room temperature.
- Ensure correct endotracheal tube (ETT) position.
- Check ETT length at lips.
- Listen for bilateral air entry and look for chest movement.
- If in doubt, ensure ETT in trachea using laryngoscope and adjust to ensure bilateral equal air entry.
- Chest X-ray not necessary before first dose.
- Refer to manufacturer's guidelines and Neonatal Formulary.
- Invert surfactant vial gently several times, without shaking, to resuspend the material.
- Draw up required dose.
- Administer via TrachCare Mac™ device or specific surfactant administration pack.

SUBSEQUENT MANAGEMENT

- If baby remains ventilated at $\text{FiO}_2 > 0.3$ with mean airway pressure > 7 cm H₂O, give further dose of surfactant 6–12 hr after first dose, repeat 100 mg/kg (1.25 mL/kg), Maximum 2 doses at doses at 12 hour gap.
- Third dose should be given only at request of attending consultant.

INSTALLATION

- With baby supine, instil prescribed dose down ETT.
- Wait for recovery of air entry/chest movement and oxygenation between boluses.

POST-INSTALLATION CARE

- Do not suction ETT for 8 hr following instillation of surfactant.
- Be ready to adjust ventilator/oxygen settings in response to changes in chest movement, tidal volume and oxygen saturation. Use of volume-target ventilation can facilitate responsiveness to rapid changes in lung compliance following surfactant instillation. Be ready to reduce FiO_2 soon after administration of surfactant to avoid hyperoxia.
- Take an arterial/capillary blood gas within 30 minutes.

DOCUMENTATION

- For every dose given, document in case notes:
- Indication for surfactant use.
- Time of administration.
- Dose given.
- Condition of baby pre-administration, including measurement of blood gas unless on labour ward when saturations should be noted.
- Response to surfactant, including measurement of post-administration blood gas and saturations.
- Reason(s) why second dose not given, if applicable.
- Reason(s) for giving third dose if administered.
- Prescribe surfactant on drug chart.



SURFACTANT REPLACEMENT THERAPY - LESS INVASIVE SURFACTANT ADMINISTRATION (LISA)



LESS INVASIVE SURFACTANT ADMINISTRATION (LISA)

Definition

- Method using a thin catheter to deliver surfactant in spontaneously breathing preterm infant with respiratory distress syndrome receiving non-invasive ventilator support
- Continue non-invasive ventilator support during procedure

Indication

- Suspected surfactant deficiency leading to respiratory distress syndrome on non-invasive respiratory

Support as evidenced by:

- Rapidly increasing oxygen requirements
- FiO₂ > 0.3
- Increased work of breathing (exclude pneumothorax by transillumination of chest)
- < 33 weeks' gestation
- Aged < 48 hour

Exclusion: Persistent/worsening respiratory acidosis despite optimal non-invasive ventilation

Equipment

- Laryngoscope/video laryngoscope
- Suction
- Sterile gloves
- LISA catheter (LISAcath®)
- Surfactant, and syringe and needle to draw up surfactant

Drugs

- Inj. Fentanyl 0.7 mcg/kg (awake sedation)
- Inj. Atropine 20 mcg/kg
- Inj. Naloxone 100 mcg/kg (if poor respiratory effort after procedure)

Emergency equipment

- Bag/valve/mask/T-piece
- Oxygen and air
- Stethoscope
- ETTs

Poractant alfa

Curosurf®

suspension for intratracheal administration 1.5 ml (80 mg/ml)

Chiesi

LISAcath®

Procedure

- Determine and document indication for LISA
- Ensure baby is loaded/on caffeine (spontaneous breathing extremely important for LISA)
- Inform parents (if present)
- Ensure venous access (peripheral cannula)
- Ensure team of 3 for procedure (including at least 1 nurse and 1 doctor)
- Draw up surfactant 200 mg/kg
- Attach T-piece to end of syringe with Luer-lock system
- Wash hands and use sterile gloves
- Place baby supine, ensuring incubator doors do not limit movement of laryngoscope
- Minimise heat loss:** if necessary, increase incubator temperature, use blankets, swaddling and transwarmer
- Baby will remain on non-invasive ventilation support (CPAP/HFNC) during procedure – have naso/orogastric tube in situ to help identify oesophagus
- Administer sedation:** Inj. atropine and Inj. fentanyl IV
- Visualise vocal cords** using laryngoscope/video laryngoscope (some gentle cricoid pressure may be necessary)
- Insert LISAcath® until required markings (see Table & image below) - tip should be 1.5 cm below vocal cords
- Other guidance according to gestational age and weight.

Table

Gestational Age (week)	Current Weight (kg)	LISAcath® length at lips (cm)
23–24 weeks	0.5–0.6	5.5
25–26 weeks	0.7–0.8	6.0
27–29 weeks	0.9–1.0	6.5
30–32 weeks	1.1–1.4	7.0
32–33 weeks	1.5–1.8	7.5

- Close mouth around LISAcath® with your fingers, ensuring not to apply any pressure on soft tissue
- Maintain LISAcath® in midline position to avoid traumatising mucosal lining of trachea

This is not an emergency procedure. Stop if you are having difficulty and consider alternatives

- Ask helper to administer surfactant in 4 aliquots very slowly (with gaps of 30 seconds over 3–5 min), to avoid surfactant coming back up
- Remove LISAcath® and ensure baby clinically stable with normal cardiorespiratory parameters before repositioning baby and closing incubator
 - Following procedure, document:
 - procedure
 - tolerance
 - FiO₂



NEONATAL JAUNDICE

TYPES OF NEONATAL JAUNDICE

Features	Physiological neonatal jaundice	Pathological neonatal jaundice
Type of hyperbilirubinemia	Always unconjugated hyperbilirubinemia	Can be either conjugated or unconjugated hyperbilirubinemia
Onset	> 24 hours after birth	Can present < 24 hours after birth
Peak total serum bilirubin	< 15 mg/dL (in the case of a full-term, breastfed infant)	May rise > 15 mg/dL
Daily rise in bilirubin levels	< 5 mg/dL/day	> 5 mg/dL/day
Etiology	Hemolysis of fetal hemoglobin and an immature hepatic metabolism of bilirubin	↑ production of bilirubin, ↓ conjugation, Impaired excretion, ↑ enterohepatic circulation

SUBTYPES AND VARIANTS

Breast-feeding jaundice

- Pathophysiology: insufficient breast milk intake; → lack of calories and inadequate quantities of bowel movements to remove bilirubin from the body → ↑ enterohepatic circulation increased reabsorption of bilirubin from the intestines → unconjugated hyperbilirubinemia
- Clinical features: onset within 1 week
- Treatment: Increase breastfeeding sessions, rehydration

Breast-milk jaundice

- Pathophysiology: increased concentration of beta-glucuronidase in breast milk → ↑ deconjugation and reabsorption of bilirubin → persistence of physiologic jaundice with unconjugated hyperbilirubinemia
- Clinical features: onset within 2 weeks after birth; lasts for 4–13 weeks
- Treatment: Continued breastfeeding and supplementation with formula feeds. Phototherapy, if required

Clinical features

Yellow discoloration of the skin and the mucosa is caused by accumulation of excess bilirubin in the tissue and plasma (serum bilirubin should be in excess 7 mg/dL). A value >15 mg/dL is considered severe. About 80% of term newborn and most preterm newborns develop clinical jaundice.

Physical examination for icterus: The American Academy of Pediatrics (AAP) recommends regular assessment of all neonates for jaundice (every 8–12 hours) while in the hospital

Symptoms

- Look for symptoms of an infective cause.
- Neurological symptoms indicate kernicterus.

Signs

- Yellow skin and sclera (it is not possible to accurately assess level of bilirubin from how jaundiced a child looks; you must get lab levels)
- Hepatomegaly (hepatic, infective, metabolic causes)
- Hepatosplenomegaly (haemolytic causes).
- Pallor/Pale conjunctiva (if haemolytic cause).

Diagnostic workup

- Serum bilirubin test: Transcutaneous bilirubin measurement (TcB) and serum bilirubin test
- CBC: reticulocyte count, Haematocrit
- Blood group (ABO, Rh) status—mother & infant
- Direct coombs' test
- Markers of inflammation: ESR, CRP, Albumin
- Total serum protein and serum albumin
- Thyroid status: TSH and free T4
- G6PD activity (in patients with G6PD deficiency)
- Septic profile (see neonatal sepsis)
- Blood culture and urine culture for infection

Rx

- Supportive therapy** – Most jaundiced babies (especially term) do not require treatment. The baby is given more frequent breast feeding. In premature babies, careful observation is required and evidences of rising bilirubin near critical level need exchange transfusion. Treatment is targeted at reducing the risk of kernicterus and hence permanent neurological sequelae.
- Phototherapy:** Reduces unconjugated bilirubin
 - Special 'Blue light' with an output of 420–480 nm wavelengths are the most effective and has the ability to convert toxic unconjugated bilirubin to non-toxic.
 - Double Phototherapy** (overhead light-plus light from below or fiberoptic blanket) is twice as effective as single phototherapy.
 - Phototherapy should be started early, exposing the maximum surface area and shielding the eyes. It may be continuous or interrupted for breastfeeding.
- Exchange Transfusion:** Most rapid method for lowering serum bilirubin concentrations. **Venesection:** baby's blood volume removed **PLUS Blood transfusion**
- IV Immunoglobulin (IVIG)**
 - Indications:** Used in cases with immunologically mediated conditions, or in the presence of Rh, ABO, or other blood group incompatibilities that cause significant jaundice
 - IVIG Dosage:** 500–1000 mg/kg
- IV fluids therapy:** Should be given to those neonates who are clinically dehydrated or who have a Total serum bilirubin (TSB) approaching the Exchange transfusion level by 2mg/dl or with a rapidly rising bilirubin (>0.5mg/dl/hr) and monitor input/output
- Correct underlying cause:** Sepsis, seizures, hypoglycemia
- Phenobarbital therapy** induces hepatic microsomal enzymes and increases bilirubin conjugation and excretion.
- If indicated:** Prevention by Protein-rich nutrition in the form of breast milk or special formula feeds and Liver transplant

GUIDELINES FOR PHOTOTHERAPY & EXCHANGE TRANSFUSION

PHOTOTHERAPY

Phototherapy is the primary treatment in neonates with unconjugated hyperbilirubinemia

Indications

- For infants born ≥ 35 weeks gestation, threshold bilirubin levels for treatment are based on the American Academy of Pediatrics (AAP) phototherapy nomogram, which divides the infants into three risk groups:
 - Low-risk infants: ≥ 38 weeks and well
 - Medium-risk infants: ≥ 38 weeks with risk factors (isoimmune hemolytic disease, G6PD deficiency, sepsis), or 35-37 weeks & well
 - High-risk infants: 35-37 weeks with risk factors
- For infants born < 35 weeks gestation, threshold bilirubin levels for treatment are lower because premature infants are at a greater risk of neurotoxicity.

Procedure

- Exposure to blue light (non-UV, wavelength: 420-480 nm) $\rightarrow$ photoisomerization (major mechanism) and photooxidation (minor mechanism) of unconjugated (hydrophobic) bilirubin in skin to water-soluble forms $\rightarrow$ excretion of water-soluble form in urine &/or bile
- Continued until total bilirubin levels < 15 mg/dL
- Adequate fluid supplementation to prevent dehydration
- Eye protection to prevent retinal damage

Contraindications

- Concomitant use of photosensitizing medications
- Congenital erythropoietic porphyria
- Family history of porphyria

Side effects

- Diarrhea, dehydration
- Changes in skin hue (bronzing) & skin rashes
- Separation of the neonate from the mother
- Increase Risk of AML
- Bronze Baby Syndrome (Rare)
 - Occurs in infants with elevated direct bilirubin (conjugated bilirubin > 2 mg/dL) following phototherapy
 - Thought to be caused by abnormal accumulation of bronze-colored pigments (photoisomers of bilirubin) within the skin
 - Presents with a reversible grayish-brown discoloration of the skin, urine, and serum
 - Usually resolves slowly after cessation of phototherapy without complications

EXCHANGE TRANSFUSION

Most rapid method for lowering serum bilirubin concentrations

Indications

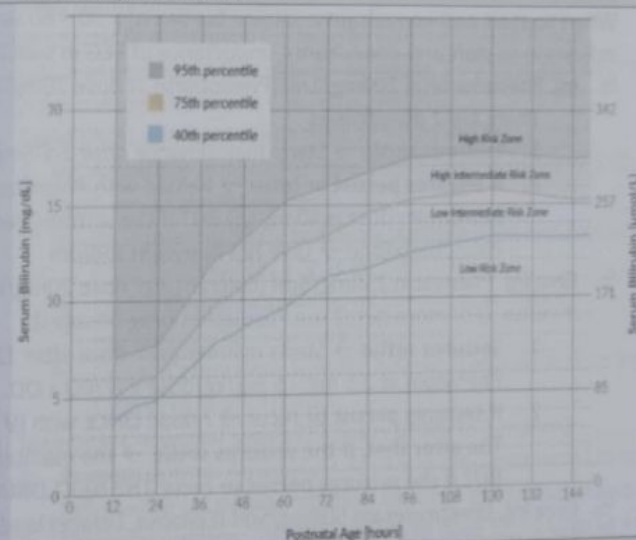
- Threshold in a 24-hour-old term baby is a total serum bilirubin value > 20 mg/dL
- Inadequate response to phototherapy, or a rapid rise in the total serum bilirubin level (> 1 mg/dL/hour in less than 6 hours)
- Acute bilirubin encephalopathy
- Hemolytic disease, severe anemia

Procedure

- Use ABO-matched and Rh-negative erythrocyte concentrate.
- Exchange blood in quantities of 5-20 mL via an umbilical venous catheter until total serum bilirubin is < 95 th percentile on nomogram.

Side effects

- Higher mortality and morbidity from infections
- Acidosis
- Thrombosis
- Hypotension
- Electrolyte imbalances



Bhutani nomogram

- The Bhutani nomogram defines age-specific percentile curves to evaluate the risk of developing pathological neonatal jaundice.
- Depending on the measured serum bilirubin value, several risk zones are defined. Neonates in the high risk zone must be evaluated for pathological jaundice!



Neonatal phototherapy: Neonate under a phototherapy lamp. Except for the diaper and socks, the neonate is undressed to expose the greatest skin surface area. The phototherapy goggles protect from potential retinal damage. Source: "Bili light with newborn".

NEONATAL SEIZURES

TREATMENT OF NEONATAL SEIZURES



Rx

- ☞ Stabilize patients using ABCD&E approach.
- ☞ Establish intravenous (IV) access.
- ☞ Vitals monitoring: BP, PR, RR, Temp. & check SpO₂ → Give high flow O₂ as needed, aim to keep SpO₂ 94–98%.
- ☞ Obtain labs: CBC, urea, creatinine, electrolytes, LFTs, Blood sugar level, calcium, magnesium, phosphorus, culture (blood, urine) and consider lumbar puncture for CSF analysis and culture.
- ☞ Correction of underlying cause
 - » If Hypoglycemia (Blood sugar level <40 mg/dL): Administer IV Dextrose 10% at dose 2–4 ml/kg x IV as bolus, followed by continue maintenance infusion 6–8 ml/kg/min to maintained at BSL at 70–100 mg/dL.
 - » If Hypocalcemia (total Ca <1.7 mmol/L or ionised Ca <0.64 mmol/L): Administer calcium gluconate 10% at dose 0.5 to 2 mL/kg x IV over 5–10 min with cardiac monitoring, followed by oral calcium (Calcium-P) at dose 40–50 mg/kg/day for few days.
 - » If Hypomagnesaemia (<0.68 mmol/L): Administer IV magnesium sulphate at dose 100mg/kg (0.4–0.6mEq/kg) x IV or deep IM (also use for refractory hypocalcemic fit)
 - » Suspected Infection: Appropriate antibiotic therapy following complete septic work-up
 - » To relieve raised intracranial pressure: 20% Mannitol at dose 0.5–1mL/kg is given IV over 30–60 minutes.
- ☞ To control seizures: Anticonvulsive: IV Phenobarbitone, IV Phenytoin and IV Levetiracetam.
- When to start anti-convulsants: Seizure burden of > 30–60 second per hour should be considered as an indication to start anti-convulsants, importance of EEG in subclinical seizures.
- ☞ Inj. Phenobarbital 200mg/1ml (Phenobarb) at dose 20mg/kg x IV over 15–20 minutes
 - There are 2 possibilities
 1. Seizures settle → Starts maintenance dose 2.5–5mg/kg/dose x IV/PO x OD after 12hour.
 2. If seizures persist or recur → Reload with Phenobarbitone 10mg/kg/dose x IV over 5–10 minutes (Maximum dose is 40mg/kg) BUT if the seizures persist or recur after maximum dose of Phenobarbitone → Give IV Phenytoin sodium
 - ☞ Give Inj. Phenytoin 250mg/5ml (Epigran) x at dose 20mg/kg/dose in 50–100ml 0.9% N/S x IV over 20 minutes. (For more detail see Paediatrics drug dosages)
 1. Seizures settle → Starts maintenance dose after 12 hours in a COMBINATION Phenobarbitone and Phenytoin at 2.5 mg–5 mg/kg/dose x IV/PO x OD.
 2. If seizures persist or recur → reload ONCE with IV Phenytoin at dose 10mg/kg over 20 minutes. The after that, If the seizures settle → the maintenance need to be started after 12 hours BUT if the seizures persist or recur THE NEXT DRUG should be given → Levetiracetam
 - ☞ Give Inj. Levetiracetam 500mg/5ml (Epilapsa, Lerace) loading dose 10mg/kg/dose diluted in 20–30ml of 0.9% NS or Dextrose 5% x IV Over 15 minutes → There are 2 possibilities
 1. Seizures settle → starts maintenance with all THREE DRUGS Levetiracetam 10mg/kg, Phenobarbitone & Phenytoin at 2.5mg–5mg/kg x IV/PO x OD after 12hour.
 2. If seizures persist or recur → Give Inj. Pyridoxine (Neurobion)
 - ☞ Inj. Pyridoxine 50–100mg x IV Slow Infusion, EEG monitoring, can be given to babies unresponsive to conventional anticonvulsants or seek neurologist opinion.
 1. If The Seizures Settle → Continue Pyridoxine 15–30mg/kg/day x OD lifelong (Max 500mg/kg/day)
 2. IF THE SEIZURES PERSIST Inj. Midazolam 5mg/5ml (Dormicum) at dose 0.1–0.4mg/kg/hour x IV Infusion and prepare for mechanical ventilation.
 - ☞ Transfer to PICU: Consider induction of Anesthesia (Propofol, Thiopental + Midazolam)
 - ☞ Correct underlying cause: hypoglycemia, hypocalcemia, electrolytes abnormalities and infection (sepsis)
 - ☞ Monitoring: Pupillary reflexes, GCS level, input/output record
 - ☞ Obtain radiological investigation: Ultrasonography of the head, CT Brain or MRI Brain, EEG (Best)

Reference: The ILAE classification of seizures and the epilepsies, Textbook of Paediatrics emergency medicine

NEONATAL SEPSIS

Clinical features

- ☛ **Risk factors:**
 - ☛ **Maternal:** Fever, PROM, premature labor, Infections (e.g., UTI)
 - ☛ **Fetal:** Premature birth, low birth weight, low Apgar score, Difficult delivery, Asphyxia
- ☛ **Non-specific features**
 - ☛ Irritability, lethargy, poor feeding, poor sucking, poor cry
 - ☛ **Temperature changes** (fever and hypothermia both possible)
 - ☛ **Cardiovascular:** tachycardia, hypotension, poor perfusion, and delayed capillary refill > 3 sec
 - ☛ **Respiratory:** tachypnea, dyspnea (e.g., expiratory grunting), apnea (more common in preterm infants)
 - ☛ **Skin tone:** jaundiced and/or bluish-gray (indicates poor perfusion)
- ☛ **Specific symptoms:**
 - ☛ **CNS:** irritability, vacant stare, seizures, hyporeflexia, hypotonia, shrill cry
 - ☛ **CVS:** Hypotension, poor perfusion, mottling and shock.
 - ☛ **Respiratory:** apnea, tachypnea, retraction, grunt, cyanosis
 - ☛ **GIT:** Feed intolerance, diarrhea, ileus, Neonatal enterocolitis (NEC)
 - ☛ **Liver:** Jaundice, hepatomegaly
 - ☛ **Blood:** pallor, petechiae, purpura, Bleeding, splenomegaly
 - ☛ **Skin:** multiple pustules, abscess.

Diagnostic workup

- ☛ **Blood culture** should be done before antibiotics. Three blood samples from different sites for blood culture.
- ☛ **Urine culture (suspected UTI)**
- ☛ **Urinalysis:** nitrites &/or leukocytes if UTI
- ☛ **CBC:** Leukocytopenia or leukocytosis, thrombocytopenia
- ☛ **Serum CRP and ESR:** Elevated
- ☛ **Serum lactate & creatinine:** Elevated
- ☛ **LFTs & Serum electrolytes:** Abnormal
- ☛ **Lumbar puncture:** CSF analysis & culture
- ☛ **Chest x-ray:** possible pneumonia

Septic screen: Panel of test 5 Parameter

1. **WBC count:** <5000 to >34000/mm³
2. **Absolute neutrophils count (ANC):** <1500/mm³
3. **Micro ESR:** ≥15mm in 1st hour
4. **CRP:** > 1mg/dl
5. **Immature to total neutrophil ratio:** ≥20%



TREATMENT OF NEONATAL SEPSIS

- ☛ **Stabilize patient using ABCD&E approach**
- ☛ **Establish intravenous (IV) access**
- ☛ **Vitals monitoring:** BP, PR, RR, Temperature and check SpO₂ → Give high flow O₂ as needed, aim to keep SpO₂ 94-98%
- ☛ **Obtain labs:** CBC, urea, creatinine, electrolytes, LFTs, Blood sugar level, procalcitonin, lactate, CRP, ESR, culture (blood, urine), Chest X-ray, Urine & stool analysis, CT scan brain plain if altered mental status and consider lumbar puncture (LP) for CSF analysis & culture.
- ☛ **Haemodynamic support:**
 1. **IV fluid administration with 0.9% NS** 10mL/kg (20mL/kg in infant) bolus as a push, then reassess, if required repeat as needed, to a maximum total volume of 40 mL/kg. Repeat assessment of fluid status. **PERFUSION** (Heart rate, capillary refill time, urine output), clinical condition and assessment for signs of fluid overload.
 2. **Consider inotropic agent:** if haemodynamic instability persist despite after 40mL/kg fluid resuscitation, start **Inj. Dopamine IV infusion** at dose 5 mcg/kg/minute and titrate upto 20 mcg/kg/minute as needed)
- ☛ **Prophylactic IV antibiotics:** No need to wait for culture report, Duration of antibiotics for **culture – ve sepsis** 5 – 7 days and 10 – 14 days for **culture + ve sepsis** without meningitis.
 - ☛ **Early-onset neonatal sepsis (first 72 hours of life)**
 1. **Inj. Ampicillin** (Amplus) at dose 100-200mg/kg/day x IV x TDS
 2. **PLUS** one of the following:
 - ☛ **Inj. Amikacin** 50mg or 100mg/ampule (Gracil or Amkay) at dose 15mg/kg/day x IV, once daily (OD)
 - ☛ **OR Inj. Gentamicin** 40mg/ml (Genticin) at dose 4 mg/kg/day x IV, once daily (OD)
 - ☛ **OR Inj. Cefotaxime** 1g/vial (Claforan, Cefotax) at dose 100-150mg/kg/day x TDS/BD
 - ☛ **Late-onset neonatal sepsis (72 hours of life to 1 month)**
 - ☛ **Primary option:** Ampicillin + Amikacin OR Gentamicin OR Inj. Cefotaxime (as dosage mention above of early onset sepsis)
 - ☛ **Secondary option:** Inj. Vancomycin at dose 10 – 15mg/kg x BD **PLUS**, Gentamicin OR Cefotaxime (as above dosage)
- ☛ **If seizures:** **Inj. Midazolam** 5mg/5ml (Dormicum) at dose 0.1 to 0.4mg/kg/dose x IV slow (**Maximum dose 10mg**)
- ☛ **Positioning and temperature maintenance (warmth)**
- ☛ **Monitoring:** Pupillary reflexes, GCS level, input/output record
- ☛ **Correct electrolytes imbalance**
- ☛ **Correct underlying cause:** i.e UTI, pneumonia, meningitis
- ☛ **Investigation:** Chest X-ray, Urine & stool analysis, Urine culture, CSF analysis, CT scan brain plain if altered mental status

CHOICE OF EMPIRICAL ANTIBIOTICS MUST BE BASED UPON LOCAL DATA OF ETIOLOGICAL ORGANISM & THEIR ANTIBIOGRAM

- 1st line: **Inj. Ampicillin/Salbutam** (Ambac) **PLUS** Gentamicin or Amikacin
- 2nd line: **Inj. Ampicillin/Salbutam** (Ambac) **PLUS** Cefotaxime (Claforan)
- 3rd line as well in resistance cases: **Inj. Piperacillin/Tazobactam** + Amikacin
- 4th line: **Inj. Meropenem** or **Inj. Imipenem** **PLUS** Vancomycin (if MRSA)



OMPHALITIS (UMBILICAL SEPSIS)

Definition: Omphalitis is an infection of the umbilicus and/or surrounding tissues, occurring primarily in the neonatal period. It is a true medical emergency that can rapidly progress to systemic infection and death, with an estimated mortality rate between 7 and 15 percent. Early recognition and treatment are essential to prevent the morbidity and mortality associated with omphalitis.

Etiology

- » Bacterial infection of the umbilical stump occurring 3–9 days after delivery
- » **Pathogens:** *Staphylococcus aureus*, group A *Streptococcus*, *E. coli*, *Klebsiella pneumoniae*
- » ***Clostridium tetani* (anerobic):** common cause of omphalitis and neonatal tetanus in developing countries

Risk factors: low birth weight, prolonged labor, maternal infection

Clinical features:

- » Base of the cord stump looks moist and the periumbilical skin becomes red, tender and swollen
- » **Discharge:** serous or seropurulent umbilical discharge which may be offensive.
- » There is delay in falling off of the cord.
- » **Signs of systemic infection:** include pyrexia and features of toxemia or jaundice in severe infection.

Spread of infection: (1) Periumbilical cellulitis with suppuration; (2) Thrombophlebitis of the umbilical vein with extension of the infection to the liver producing hepatitis or pyaemic liver abscess; (3) Peritonitis; and (4) Necrotizing fasciitis and rarely myonecrosis (infectious muscle involvement) associated with high mortality rates

Diagnostic workup

» Generally Clinical diagnosis » Umbilical swab culture » CBC: Leukocytopenia or leukocytosis, thrombocytopenia » Serum CRP and ESR: Elevated » In systemic infection: Blood Culture (Sepsis) and Lumber puncture: CSF analysis & culture (meningitis)	Septic screen: Panel of test 5 Parameter 1. WBC count: <5000 to >34000/mm³ 2. Absolute neutrophils count (ANC): <1500/mm³ 3. Micro ESR: ≥15mm in 1st hour 4. CRP: > 1mg/dl 5. Immature to total neutrophil ratio: ≥20%
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TREATMENT OF OMPHALITIS (UMBILICAL SEPSIS)

Prevention

- » Keep the navel dry (frequent diaper change)
- » Observe general hygiene measures
- » Regular wound dressing

Prophylactic IV Antibiotics:

- » Initial empiric treatment with antistaphylococcal penicillin and aminoglycoside is recommended.
- » **Antistaphylococcal penicillin:** Inj. Piperacillin/tazobactam 2.25mg/vial or 4.5g/vial (Tanzo, Tazocin EF) children's age >2–9 months at dose 80–100mg/kg (based on piperacillin component) IV every 8 hours (TDS) OR Inj. Nafcillin 2g/vial 25mg/kg/dose IV/IG every 12 hours
- » **PLUS Inj. Amikacin 50mg or 100mg/ampule** (Gracil or Amkay) at dose 15mg/kg/day x IV, once daily (OD) OR Inj. Gentamicin 40mg/ml (Genticin) at dose 4–5mg/kg/day x IV, once daily (OD)
- » Consider the addition of an antibiotic with anti-MRSA activity: vancomycin at dose 10mg/kg IV every 6 hours
- » Consider for anerobic cover (If there is suspicion for maternal chorioamnionitis or the patient has a foul-smelling discharge from the stump): Metronidazole OR Clindamycin 7.5 mg/kg/dose IV every 8 hours
- » **Duration of therapy:** The duration of antibiotic therapy depends on the patient's clinical response and any complications that may develop during hospital admission. For uncomplicated cases of omphalitis, the recommended course of parenteral therapy is 7–10 days, followed by a switch to oral antibiotic therapy (cephalexin suspension at dose 50 mg/kg/day divided, every 8 hour) depending on culture results.
- » **For fever:** Inj. Paracetamol 1g/100ml (Provas) at dose 15 mg/kg/dose x three or four time a day

ACUTE TONSILLITIS

Definition: It is an inflammatory process of the tonsillar tissues and is usually infectious in nature. Acute infections of the tonsils predominantly occur in school-aged children, but patients of any age may be affected. Tonsillitis of viral origin is usually not required antibiotics therapy and treated with supportive care.

Most common cause-viral infections: Tonsillitis initially starts with viral infection followed by secondary bacterial infection.

Risk factors:

- Most commonly seen in school going children between 5 – 15 years of age.
- Contact with infected people in enclosed spaces (school, care centres)

Clinical features

Symptoms: The leading symptoms tend to be mild & non-specific, and include:

- Pain on swallowing
- Fever > 100.5 °F (> 38°C)
- Sudden onset of sore throat.
- Malaise, Headache
- Cough (dry) in one third patients
- Particularly in very young children, feeding may be affected.

Signs

- Tonsillar exudates
- Tonsillar erythema/redness
- Tonsillar enlargement
- Enlarged & tender ant. cervical lymph nodes

Diagnostic Workup

- Throat culture is definitive diagnostic test of bacterial tonsillitis.
- Rapid streptococcal antigen test → high probability of group 'A' beta-hemolytic streptococci (GABHS) infection in children >3 years old and adult's patient.
- CBC: Raised WBC count with neutrophilia is suggestive of a bacterial infection, whereas an elevated WBC count with lymphocytosis and atypical lymphocytes is suggestive infectious mononucleosis (Heterophile antibody testing)

Choice of antibiotics:

- Drug of choice: Penicillin, Co-Amoxiclav
- Patients allergic to penicillin can be treated with macrolides: Erythromycin OR Clarithromycin.
- Other: Cephalexin, Cefadroxil

Duration of treatment: 5 – 10 days

Rx

Self-limited infective condition that normally resolves completely within 1 week with no sequelae and do not require antibiotics.

Use of antibiotics:

- Reduce the duration and severity of symptoms
- Prevent suppurative and non-suppurative complications
- Prevent rheumatic fever.
- Reduce transmission of infection.

Patient are kept on bed rest.

Encourage good oral hydration and food intake.

Steam inhalation may be benefited.

Recommended antibiotics: 156.25mg/5ml (Augmentin, Calamox)

1. Symp. Co-Amoxiclav 312.50mg/5ml (Augmentin DS, Calamox DS)

Dosage: 25 – 40 mg/kg/day x TDS/BD (8 – 12 hourly) x 10 days

OR Symp. Azithromycin 200mg/5ml (Azomax, Zetro, Azitma)

Dosage: 10mg/kg x once daily for 5 days (Maximum: 500mg/day)

OR Symp. Clarithromycin 125mg/5ml, 250mg/5ml (Claritek, Klaricid)

Dosage: 15mg/kg/day x twice daily x 10 days (Max dose: 1g/day)

OR Symp. Cephalexin 125mg/5ml OR 250mg/5ml (Ceporex, Keflex)

Dosage: 30mg/kg/day x twice daily x 10 days (Max dose: 2g/day).

OR Symp. Cefadroxil 125mg/5ml OR 250mg/5ml (Cedrox, Duricef)

Dosage: 30mg/kg/day x twice daily x 10 days (Max dose: 2g/day).

For fever/analgesia: (Calpol 6 Plus, Panadol forte = 250mg/5ml)

2. Symp. Paracetamol (Calpol = 120mg/5ml, Panadol = 160mg/5ml)

Dosage: 10 – 15mg/kg/dose x TDS/QID. (Maximum: 75 mg/kg/day)

OR Symp. Ibuprofen (Brufen = 100mg/5ml, Brufen DS = 200mg/5ml)

Dosage: 10mg/kg/dose x TDS/QID (Maximum dose: 40mg/kg/day)

If symptoms of allergy, hay fever, cough & common cold.

3. Symp. Dextromethorphan + Chlorpheniramine Maleate (Babynol)
5 – 10ml (1-2 teaspoonful) x TDS

RECURRENT EPISODES OF TONSILLITIS

Tonsillectomy may be considered for patients who have recurrent symptoms of tonsillitis that do not become less common with time and for whom there is no other explanation for the recurrent symptoms.

In its guideline for children ages 1-18 years, the American Academy of Otolaryngology-Head and Neck Surgery recommends watchful waiting for recurrent throat infection if there have been less than seven episodes in the past year, less than five episodes per year in the past 2 years, or under three episodes per year in the past 3 years. In children, tonsillectomy can reduce days and number of episodes of sore throat in the first year. More benefit was reported in those children who were more severely affected.

Tonsillectomy in children is also associated with significant improvements in quality of life compared with watchful waiting. Tonsillectomy is also indicated in children with additional exacerbating factors such as obstructive sleep apnea, peritonsillar abscess, and periodic fever, aphthous stomatitis, pharyngitis, adenitis (PFAPA) syndrome.

PLUS antibiotics course for prevention of complications (as mention above)

ACUTE EPIGLOTTITIS

- ☛ **Etiology:** Commonly *Haemophilus influenzae* type-B (Hib). Most cases now involve: *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Staphylococcus aureus*, Nontypeable *H. influenzae*

Clinical features

- » Acute onset of high fever 102–104°F (39–40°C)
- » The patient looks unwell.
- » Tripod position: eases respiration as the airway diameter is increased by leaning forward and extending the neck in a seated position
- » Sore throat, Absence of cough
- » The hallmarks features are the 3D's: Dysphagia, Drooling, and Distress.
- » Muffled voice (resembling a "hot-potato" voice) with painful speech
- » Respiratory Distress: Nasal flaring, tracheal tug, raising the shoulders, cyanosis, intercostal recession, and inspiratory stridor is a late sign, which indicates upper airway narrowing.
- » Restlessness and/or anxiety
- » General examination may elicit cervical lymphadenopathy and tenderness to palpation over larynx/throat



Source: Khaleel M. Elsayes, Sandra A. A. Oldham: *Introduction to Diagnostic Radiology*; www.accessmedicine.com
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Diagnostic workup

- ☛ **Gold standard test:** Indirect laryngoscopy or flexible fiberoptic laryngoscopy (should be performed in an area that has access to an emergency airway) – shows Cherry-red epiglottis, Pooled secretions, Inflammation and edema of the supraglottic structure
- ☛ **X-Ray neck lateral view:** Thumbprint sign (enlarged epiglottis and supraglottic narrowing)
- ☛ **Swab of the epiglottis and epiglottic culture:** to guide antibiotic therapy
- ☛ **Confirm infective cause:** CBC, CRP, swabs of epiglottitis for epiglottic culture blood culture.

Rx

TREATMENT OF ACUTE EPIGLOTTITIS

- ☛ **Stabilize patient using ABCD&E approach**
 - » Keep the patient calm and sitting upright position to prevent further airway compromise.
 - » Assess and secure stable airway, to prevent impending complete obstruction. Clinical features of obstruction (e.g., stridor, tachypnea, retractions, hypercapnia, cyanosis, loss of air movement, altered mental state)
 - » Check for SpO₂, if <94 administer O₂ therapy via through a non-rebreather mask. Aim to keep SpO₂ 94–98%.
 - » Patients with clinical features of airway obstruction or risk factors for acute deterioration
 - ↳ If there are signs of acute respiratory distress, begin bag-mask ventilation with 100% oxygen.
 - ↳ Consider racemic epinephrine in otherwise healthy adults as a temporizing measure until a definitive airway is established.
 - ↳ Secure the airway with emergency endotracheal intubation in a controlled setting by experience doctor
 - ↳ Prepare to perform an emergency surgical airway if endotracheal intubation is unsuccessful.
- ☛ **Establish intravenous (IV) access (IV cannula)**
- ☛ **Vitals monitoring:** BP, PR, RR, temperature, and SpO₂
- ☛ **Obtain investigations:** CBC, CRP, blood sugar level swabs of epiglottis for epiglottic culture and blood culture.
- ☛ **IV fluid resuscitation:** Isotonic fluids at dose 20–30 mL/kg (R/L or N/S 0.9%) as the patient is nil by mouth (NPO)
- ☛ **First line IV empirical antibiotic:** coverage to include gram positive cocci and *haemophilus influenzae*-type-B. IV antibiotics should be continued for 2–3 days, followed by oral antibiotics to complete a 10-day course.
 - » Inj. Ceftriaxone 1g/vial (Rocephin, Titan) at dose 50mg/kg IV every 24 hours (Max. dose 2g/24 hours).
 - » OR Inj. Cefotaxime 1g/vial (Claforan, Cefotax) at dose 150–200mg/kg/day x IV x BD/TDS
 - » OR Inj. Cefuroxime 750mg/vial (Zinacef, Zecof) at dose 50–75mg/kg/day x IV x BD/TDS
 - » OR Inj. Ampicillin-Sulbactam 1.5g/vial OR 3g/vial (Ambac) at dose 200–400mg/kg/day x IV x QID
 - » OR Inj. Piperacillin/tazobactam 2.25g/vial or 4.5g/vial (Tanzo, Tazocin EF), children's age >2–9 months at dose 80–100mg/kg (based on piperacillin component) IV every 8 hours (TDS)
- ☛ **Adjunct: Empiric corticosteroids:** Inj. Dexamethasone 4mg/ml (Decadron) at dose 0.6mg/kg x IV once
OR Inj. Methylprednisolone sodium succinate 500mg/vial (Solu-Medrol) at dose 1mg/kg/dose x IV once
- ☛ **For fever/analgesia:** Inj Paracetamol 1g/100ml (Provas) at dose 10–15mg/kg/dose x IV

CROUP (LARYNGOTRACHEOBRONCHITIS)

Definition: Acute viral inflammation of upper airway causing oedema of larynx and trachea and presenting with barking cough, stridor and respiratory distress. Over 80% of croup cases are mild.

Causative agent: Parainfluenza virus (sometimes may be influenza, respiratory syncytial virus, rhinovirus, adenovirus)

Incidence: Aged 6 months to 6 year (peak aged 2 year)

Seasonal peak: Spring and Autumn

Transmission: usually by droplet spread

Incubation period: 2 – 6 days

DIFFERENTIAL DIAGNOSIS OF STRIDOR

Acute stridor:

- » Croup, spasmodic croup
- » Epiglottitis (rare since immunization against *Haemophilus influenzae* type-B)
- » Bacterial tracheitis and Laryngeal diphtheria
- » Foreign body aspiration

Chronic stridor:

- » Allergic airways disease
- » Laryngeal haemangioma (Congenital)
- » Laryngomalacia
- » Foreign body aspiration
- » Laryngeal papilloma



Clinical features

Prodromal phase: 1–2 days of upper respiratory tract infection symptoms (rhinitis, low-grade fever, sore throat)

Symptoms of croup last 2–7 days and typically manifest in the late evening/night.

Characteristic features: seal-like barking cough, hoarseness, and inspiratory stridor due to subglottic narrowing.

» **Mild croup:** Stridor may be absent or only manifest in agitated child

» **Moderate croup**

- » Stridor and dyspnea may be present at rest.
- » Thoracic retractions are typically visible.
- » Affected individuals may be tachycardic or tachypneic.

» **Severe croup**

- » Severe stridor and dyspnea are present at rest.
- » Air entry is decreased.
- » Hypoxemia, an altered mental state, and/or other signs of impending respiratory failure may be present.
- » Upper airway obstruction can cause pulsus paradoxus.
- » Agitation can worsen symptoms and precipitate complete airway obstruction.



Source: Khaled M. Elsayes, Sandra A. A. Oldham: *Introduction to Diagnostic Radiology*; www.accessmedicine.com
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Diagnostic workup

Croup is most commonly diagnosed based on the presence of characteristic clinical features of croup.

Investigation are not routinely required; do not delay treatment in unstable patients to obtain test

X-ray chest and neck (AP and lateral): shows steeple sign (subglottic narrowing on anteroposterior view)

Confirm infective cause: CBC, CRP and ABGs (sign of respiratory distress, hypoxemia and/or Co2 retention)

Westley croup score for Croup severity assessment

Clinical features		Points	Interpretation
Level of consciousness	Normal	0	≥ 12 points: impending respiratory failure
	Disoriented	1	
Cyanosis	None	0	
	With agitation	1	
Stridor	At rest	2	8–11 points: severe croup
	None	0	3–7 points: moderate croup
	With agitation	1	
Air entry	At rest	2	≤ 2 points: mild croup
	Normal	0	
	Decreased	1	
Retractions	Markedly decreased	2	
	None	0	
	Mild	1	
	Moderate	2	
	Severe	3	

TREATMENT OF CROUP (LARYNGOTRACHEOBRONCHITIS)



- ☛ **Stabilize patient using ABCD&E approach**
 - » Keep the patient calm, minimize anxiety stress
 - » Allow the patient to maintain a comfortable position (usually semi-upright).
 - » Examine the child in the parent's lap.
 - » Avoid examining the throat as this may precipitate airway obstruction.
 - » **Hypoxemia/signs of impending respiratory failure:** Initiate immediate stabilization → supplemental oxygenation (Aim to keep SpO₂ 94-98%), intubation. Intubation in severe croup is difficult due to subglottic narrowing → anesthesiologist required!
- ☛ **Establish intravenous (IV) access (IV cannula)**
- ☛ **Vitals monitoring:** B.P, PR, RR, temperature, and SpO₂
- ☛ **Obtain investigations:** CBC, CRP and ABGs (If suspected bacterial infection – Blood culture)
- ☛ Perform a croup severity assessment to guide treatment; consider using a Westley croup score.
- ☛ Admit patients with admission criteria for croup, e.g., severe croup, age < 6 months, stridor at rest
- ☛ **Consider corticosteroids in all patients:** Inj. Dexamethasone 4mg/ml (Decadron) at dose 0.6mg/kg x IV or IM once OR Oral Prednisolone (Tab. Rapicort 5mg, Syp. Rapicort 5mg/5ml) at dose 1mg/kg for 2 days OR even nebulized dexamethasone at 0.6mg/kg in 3 mL of 0.9% normal saline.
- ☛ **Patients with moderate/severe croup:** Add nebulized racemic epinephrine (Adrenalin).
 - ☛ **Nebulized racemic epinephrine** at dose 0.5 mL of 2.25% solution diluted in 3 mL of 0.9% normal saline (Max. single dose 0.5 mL) via nebulizer OR Inj. Adrenalin 1mg/mL (1:1000) at dose 0.5mL/kg (maximum: 5mg/5ml) diluted in 3mL – 5mL 0.9% normal saline via nebulizer, dose may be repeated in 10 minute as needed.
 - ☛ **Racemic epinephrine 0.5mL (2.25%) = 5mg/6ml L-Adrenalin:** reduces airway swelling, faster onset, and improved signs of respiratory distress, airway swelling within 10 to 30 minutes than with dexamethasone.
 - ☛ 'Rebound' phenomena may occur, where the upper airway obstruction may recur as the effect of the adrenaline wears off after 1–2 hours. While in the past it was recommended that any child who received adrenaline for croup should be admitted
- ☛ **IV fluid resuscitation:** Isotonic fluids at dose 20-30 mL/kg (R/L or N/S 0.9%) as the patient is nil by mouth (NPO)
- ☛ **ANTIBIOTICS are not effective in the treatment of croup, but may be used in suspected cases of bacterial superinfection.** (e.g. pneumonia, bacterial tracheitis)
 - ☛ Inj. Ceftriaxone 1g/vial (Rocephin, Oxidil) at dose 50mg/kg IV every 24 hours (Max. dose 2g/24 hours).
 - » OR Inj. Cefotaxime 1g/vial (Claforan, Cefotax) at dose 150-200mg/kg/day x IV x BD/TDS
- ☛ **If fever/analgesia:** Inj. Paracetamol 1g/100ml (Provas) at dose 10-15mg/kg/dose x IV OR Syp. Paracetamol (Calpol = 120mg/5ml, Panadol = 160mg/5 ml) at dose 10-15mg/kg/dose x TDS
- ☛ Educate the family on concerning features, e.g., signs of respiratory distress, signs of significant dehydration.
- ☛ Regularly reassess patients, If no sustained improvement with adrenaline and dexamethasone
- ☛ Consult or referral to Paediatrics ICU for further management
- ☛ **Disposition**
 - » Discharge home with return precautions can be considered in the following cases:
 - ☛ Mild croup
 - ☛ Moderate croup that has responded to a single nebulized epinephrine treatment
 - » Patients with severe croup or other risk factors should be admitted; consider pediatric ICU.
- ☛ **Admission criteria for croup**
 - » Severe croup
 - » Need for oxygen or IV fluids
 - » 1 treatment with nebulized epinephrine
 - » Age < 6 months
 - » Persistent tachypnea or tachycardia
 - » Complex medical history (congenital cardiac or pulmonary disease, premature birth)

BRONCHIOLITIS

Clinical features	
- Initially presents with upper respiratory tract (URTI) symptoms: - Copious rhinorrhea - Low-grade fever - Cough - Followed by LRTI symptoms - On auscultation: Crackles, wheezes - Findings vary minute-to-minute as mucus is cleared and/or respiratory efforts change. - Severe illness: Respiratory distress (usually occurs in infants "<1 year of age") - Tachypnea or apnea - Prolonged expiration - Nasal flaring, grunting - Intercostal retractions - Cyanosis - Poor feeding in breastfed infants Admission criteria for bronchiolitis - Unwell appearance, lethargy - Moderate to severe signs of respiratory distress (including significantly elevated respiratory rate for age) - Ongoing respiratory support required. - Need for supplemental hydration. - History of apnea - Consider it: - Risk factors for severe bronchiolitis +ve - Supportive care at home is not feasible	TREATMENT OF MILD – MODERATE BRONCHIOLITIS - Arrange follow-up within 24 hours. - Encourage adequate feeding, oral caloric and fluid intake. - Counsel/Educate caregivers (parents) on: - If signs of deterioration and the need to seek immediate medical attention if present - How and when to provide nasal suction - The expected course of disease: The most children with bronchiolitis will recover over 7–10 days. - Advise caregivers to avoid exposing the patient to second-hand smoke; offer counseling on smoking cessation for household members. - For cough: Syp. Ivey leaf (Coferb, Olcutf) 2.5ml – 5ml x two or three time daily - Syp. Loratidine 5mg/5ml (Softin, Lorin NSA) - OR Syp. Desloratadine 0.5mg/5ml (Jordin-D, Neo-Initial) - OR Syp. Levocetirizine 2.5mg/5ml (T-Day, Neo-sedil, Ocltra) 0 + 0 + 1, 1 + 0 + 1 (2–5 years = 5mg x OD / > 5 years 5mg x BD) - Syp Paracetamol (Calpol = 120mg/5ml, Panadol = 160mg/5ml) - Dosage: 15mg/kg in three or four divided dose For fever: (Calpol 6 Plus, Panadol forte = 250mg/5ml) - Syp Paracetamol (Calpol = 120mg/5ml, Panadol = 160mg/5ml) - Dosage: 15mg/kg in three or four divided dose For Infant: - Antipyretic: Paracetamol (Panadol Infant drops 80mg/0.8ml) - Anti-allergic: Cetirizine (Rigix Infant drops 10mg/ml) - Cough suppressant: Coferb cough Drops, Hylixia cough drops TREATMENT OF SEVERE BRONCHIOLITIS - Stabilize patient using ABCD&E approach - Respiratory support and monitoring with pulse oximeter: - Supplemental oxygenation (Aim to keep SpO2 94–98%) - Adjust short-term oxygen therapy as needed. - Refractory hypoxemia, signs of respiratory distress, or resp. failure: intubation, CPAP, or high-flow nasal cannula - Vitals monitoring: BP, PR, RR, temperature, and SpO2 - Obtain investigations: CBC, RT-PCR, ABGs and chest x-ray - Consider nebulization with 3% Normal saline x 4mL/dose via nebulization every 2–8 hours; decrease frequency as tolerated. - Nebulized SAMAs: Ipratropium bromide (Atrovent 0.025%/2ml) x Children 55 years of age: 250 mcg nebulized every 6–8 hour; children 6–11 years of age: 250–500mcg every 6–8 hour
Diagnostic workup	
- Clinical diagnosis: based on the patient's age (<3 years) and classic features - Pulse oximetry: Hypoxemia - ABGs: - RT-PCR: detect viral cause - Chest x-ray: usually normal or hyperinflation, interstitial infiltrates, atelectasis or pneumonia - Investigation to exclude other causes – not routinely recommended: - Blood culture - Urinalysis and urine culture - CBC, serum electrolytes - Avoid bronchodilators, epinephrine, corticosteroids, and chest physiotherapy unless there are comorbidities (e.g., asthma, croup, cystic fibrosis, and acute otitis media). - Antibiotic therapy are not recommended in bronchiolitis. Antibiotic, may be appropriate for some children with bronchiolitis who require intubation and mechanical ventilation for respiratory failure. - Chest physical therapy is often utilized in infants with bronchiolitis in an attempt to increase the clearance of secretions and improve breathing.	

LOWER RESPIRATORY TRACT INFECTION (CHEST INFECTION)

Name:
Temperature:Age:
B.P.:Sex:
Pulse:Date:
Resp. Rate:△ LRTI (Chest infection)
C/C:

- » Fever
- » Cough and Irritability
- » Poor feeding
- » Vomiting
- » Tachypnoea at rest
(most useful sign)
- » <2 months: > 60/min
- » 2-11 months: > 50/min
- » 1-5 year: > 40/min
- » Bronchial breathing
- » Inspiratory crackles
- » Recession
- » Abdominal pain (referred
pleural pain)

Investigation:

- » CBC
- » Blood culture
- » Chest-X-ray PA view

Admit children with sats <92%,
RR >70, ↑↑ HR, ↑ CRT or
apnoea/grunting.

ILL CHILD if ANY of the following:

- » Poor perfusion
- » Altered level of consciousness
- » Respiratory failure: Hypoxia,
Hypercapnia and Acidosis

Admit to hospital

- » Resuscitate
- » Start IV antibiotics & antipyretic
- » Discuss case with PICU

Rx

1. Syp. Co-Amoxiclave 156.25mg/5ml (Augmentin, Calamox)
312.50mg/5ml (Augmentin DS, Calamox DS)
Dosage: 25-40mg/kg/day x TDS/BD (1 Teaspoonful = 5ml)
OR Syp. Cefuroxime 125mg/5ml (Zecel, Kefrox, Evorox)
Dosage: 20-30mg/kg/dose (Max: 500 mg/dose) x BD
OR Syp. Cefixime 100mg, 200mg (Cefspan, Cefiget)
Dosage: 8-10mg/kg/day x BD
1-0-1 (OD)
(Calpol 6Plus, Panadol forte =250mg/5ml)
2. Syp. Paracetamol (Calpol =120mg/5ml, Panadol =160mg/5 ml)
TDS/QID (1 Teaspoonful = 5ml)
Dosage: 10-15mg/kg/Dose
3. Syp. Anti-tussive/Cough suppressants (Hydrillin, Babynol, Corex-D)
1-2 Teaspoonful x TDS

Rx

1. Syp. Azithromycin 200mg/5ml (Azitma, Zetro, Azomax)
Dosage: 10mg/kg/day x once daily
0-0-1 (OD)
OR Syp. Clarithromycin 125mg, 250mg (Klaricid, Claritek)
Dosage: 15 mg/kg/day x BD (1 Teaspoonful = 5ml)
1-0-1 (OD)
(Calpol 6Plus, Panadol forte =250mg/5ml)
2. Syp. Paracetamol (Calpol =120mg/5ml, Panadol =160mg/5 ml)
TDS/QID (1 Teaspoonful = 5ml)
Dosage: 10-15mg/kg/Dose
3. Syp. Anti-tussive (Cough suppressants) (Hydrillin, Cofrest, Corex-D)
1-2 Teaspoonful x TDS

Rx

Neonate/infant prescription

(Augmentin, Calamox, Amclav infant drops)

1. Co-Amoxiclave 62.5mg/ml Infant drops
Dosage: 30mg/kg/day x TDS
OR Syp. Cefaclor 50mg/ml infant drops (Ceclor, Cefalor, Hiclor)
Dosage: 30-40mg/kg/dose x BD/TDS
OR Syp. Cefixime 100mg (Cefspan, Cefiget)
Dosage: 8-10mg/kg/day x BD
(Panadol (80mg/0.8ml) infant drops)
2. Paracetamol (Tempol 100mg/ml infant drops)
Dosage: 10-15mg/kg/Dose
3. Anti-tussive/cough suppressants infant drops: (Coferb, Cofif, Hylixial)
Dosage: - Children 6 months to 1 year: 12-14 drops 3 times a day

COMMUNITY ACQUIRED PNEUMONIA (CAP) – OUTPATIENT (OPD)

Clinical features

Mild/moderate pneumonia/CAP

- » Productive cough with sputum
- » Fever, Lethargy and Vomiting
- » Tachypnoea at rest (Most useful sign)
 - » < 2 months: > 60/min
 - » 2 – 11 months: > 50/min
 - » 1 – 5 year: > 40/min
- » Dyspnea
- » Bronchial breathing, Recession
- » Inspiratory crackles on auscultation
- » May be preceded by symptoms of an upper respiratory tract infection
- » Additional features may include:
 - » Abdominal pain
 - » Difficulties feeding/Poor feeding
 - » Grunting

Severe pneumonia ≥2 of following:

- » Fever >38.5°C
- » Respiratory rate >50 (>70 infant)/min
- » Cyanosis and tachycardia
- » Capillary refill time >2 second
- » Signs of dehydration
- » Severe recession
- » Not feeding and Apnoea
- » Difficulty breathing
- » Nasal flaring and Grunting

ILL CHILD if ANY of the following:

- » Poor perfusion
- » Altered level of consciousness
- » Respiratory failure: Hypoxia, Hypercapnia and Acidosis
- » Admit to Hospital
 - » Resuscitate
 - » Start IV antibiotics & IV antipyretic
 - » Discuss case with PICU

Diagnostic workup

- » CBC
- » Serum CRP/ESR
- » Serum procalcitonin
- » Chest X-ray A.P & lateral view
- » Blood culture
- » Sputum culture (difficult, routinely not performed, poor yield)

- » **Duration of treatment:** 5 – 7 days of therapy is usually sufficient for community acquired pneumonia (CAP) that is treated in the OPD. Any patient being treated in a primary care setting should be re-examined after 48–72 hours to evaluate the efficacy of the prescribed antibiotic.
- » **Additional considerations:** Knowing local resistance patterns of *S. pneumoniae* to macrolides is critical when deciding on an empiric antibiotic regimen.



Previously healthy patients without comorbidities or risk factors for resistant pathogens

Monotherapy with one of the following:

1. Syp. Amoxicillin 250mg/5ml (Amoxil, Ospomox, Princimox)
 - Dosage:** 80-90mg/kg/day x twice daily for 7 – 10 days.
 - OR Syp. Azithromycin 200mg/5ml (Azitma, Zetro, Azomax)
 - Dosage:** 10mg/kg/day x once daily for 5 days.
 - OR Syp. Clarithromycin 250mg/5ml (Klaricid, Claritek)
 - Dosage:** 15mg/kg/day x BD (1 Teaspoonful = 5ml) for 5-7 days
- For fever/analgesia: (Calpol 6 Plus, Panadol forte = 250mg/5ml)
2. Syp. Paracetamol (Calpol = 120mg/5ml, Panadol = 160mg/5 ml)
 - Dosage:** 10 – 15mg/kg/dose x TDS/QID. Maximum 75 mg/kg/day
 - OR Syp. Ibuprofen (Brufen = 100mg/5ml, Brufen DS = 200mg/5ml)
 - Dosage:** 10mg/kg/dose x TDS/QID (Maximum dose: 40mg/kg/day)
 3. For cough: Anti-tussive (Syp. Hydrillin, Syp. Cofrest, Syp. Pulmonol) 5-10 ml (1-2 Teaspoonful) x TDS/BD



Patients with comorbidities or risk factors for resistant pathogens

Combination therapy:

- » An antipneumococcal β-lactam: Amoxicillin-clavulanate or Cefuroxime or Cefpodoxime
 - » PLUS one of the following: Azithromycin or Clarithromycin.
 - 156.25mg/5ml (Augmentin, Calamox)
4. Syp. Co-Amoxiclave 312.50mg/5ml (Augmentin DS, Calamox DS)
 - Dosage:** 25-40mg/kg/day x TDS/BD (1 Teaspoonful = 5ml)
 - OR Syp. Cefuroxime 125mg/5ml (Zecel, Kefrox, Evorox)
 - Dosage:** 150mg/kg/day (Maximum: 500 mg/dose) x BD
 - OR Syp. Cefpodoxime 40mg/5ml (Prelox, Orelox, Evodoxim)
 - Dosage:** 10mg/kg/dose (Maximum: 500mg/dose) x BD
- PLUS one of the following macrolide
5. Syp. Azithromycin 200mg/5ml (Azitma, Zetro, Azomax)
 - Dosage:** 10mg/kg once daily for 5 days
 - OR Syp. Clarithromycin 125mg, 250mg (Klaricid, Claritek)
 - Dosage:** 15mg/kg/day x twice daily for 7 – 10 days
- For fever/analgesia: (Calpol 6 Plus, Panadol forte = 250mg/5ml)
6. Syp. Paracetamol (Calpol = 120mg/5ml, Panadol = 160mg/5 ml)
 - Dosage:** 10 – 15mg/kg/dose x TDS/QID. Maximum 75 mg/kg/day
 - OR Syp. Ibuprofen (Brufen = 100mg/5ml, Brufen DS = 200mg/5ml)
 - Dosage:** 10mg/kg/dose x TDS/QID (Maximum dose: 40mg/kg/day)
 7. For cough: Anti-tussive (Syp. Hydrillin, Syp. Cofrest, Syp. Pulmonol) 5-10 ml (1-2 Teaspoonful) x TDS/BD



PAEDIATRIC PNEUMONIA (CAP) – INPATIENT (WARD)

TREATMENT OF BACTERIAL PNEUMONIA IN CHILDRENS

- ☞ Stabilize patient using ABCD&E approach
- ☞ Establish intravenous (IV) access (IV cannula)
- ☞ Vitals monitoring: BP, PR, RR, temperature, and check SpO₂ if <94 administer O₂ therapy via nasal cannula: 1-6 L O₂/minutes. Aim to keep saturation 94-98%.
- ☞ Obtain investigations: CBC, urea, creatinine, electrolytes, LFTs, PT & INR, CRP, ESR, RBS and Procalcitonin
- ☞ Fluid therapy (Hydration with PO fluids or IV fluids): if unable to take oral fluids use sodium chloride 0.9% with Dextrose 5% with potassium via IV infusion. Restrict IV fluid replacement to 80% maintenance
- ☞ Correction of electrolytes imbalance and monitor electrolytes
- ☞ Empirical antibiotic therapy for pneumonia: Duration of therapy 5-7 days is usually sufficient.
 - » Inj. Cefotaxime 1g or 2g (Claforan, Cefotax) x IV x TDS at **dose** 150-200mg/kg/day
 - OR Inj. Ceftriaxone 1g/vial or 2g/vial (Titan, Rocephin) x IV x BD/OD at **dose** 75-100mg/kg/day
 - OR Inj. Cefuroxime 750mg/vial or 1.5g/vial (Zinacef, Zecef) x IV x TDS at **dose** 100-150mg/kg/day
 - » PLUS add one of the following
 - ☞ Inj. Ampicillin-Sulbactam 1.5g/vial or 3g/vial (Ambac) x IV x QID at **dose** 150-200 mg/kg/day
 - ☞ Inj. Gentamicin 40mg/ml (Genticin) x IV x OD at **dose** 7.5 mg/kg/day (WHO Guidelines)
 - » For severe ill patients/MRSA add Inj. Vancomycin 500mg/vial x IV x 6-8 hourly at **dose** 7.5 mg/kg/day
- ☞ For fever: Inj. Paracetamol 1g/100ml (Provas) at **dose** 15 mg/kg/dose x IV x TDS
- ☞ Consider nebulized Ipratropium bromide (Atrovent 0.025%/2ml) in 5-10ml 0.9% Normal saline, repeat after 4-6 hours at **dosage**: Aged <12 year: 250mcg and Aged >12 year: 500mcg
- ☞ Admit to ICU and initiate intubation if any of the following are present: signs of respiratory distress, dyspnea with hypoxemia (<90%) and tachypnea (RR > 30/min)
- ☞ Consider discharge when the following criteria are met: Clinical improvement for at least 12 hours, vital signs are stable, able to tolerate oral drugs, Caregivers are able to give medicine & there are no barriers to follow-up.

SPECIFIC ANTIBIOTICS ACCORDING GUIDELINES

☞ Hospital-acquired pneumonia	Inj. Piperacillin/Tazobactam x IV at dose 150-300 mg/kg/day
☞ Severe aspiration	Inj. Amoxicillin/clavulanic acid (Augmentin) x BD x IV at dose
☞ Effusion following aspiration pneumonia	Inj. Piperacillin + Tazobactam 4.5g (Tanzo, Tazocin EF) x IV x QID at dose 150-300 mg/kg/day
☞ Effusion following CAP	Inj. Co-amoxiclav x IV at Dosage Plus Inj. Clindamycin at dosage 30mg/kg/day x TDS x IV/PO



X-ray chest (AP view) of a child: Bilateral perihilar peribronchial thickening (examples of bronchi indicated by green lines) is accompanied by hyperinflation with diaphragmatic depression (indicated by white lines & arrow). In the right lung, a superimposed area of consolidation from pneumonia (red overlay) is associated with atelectasis and ipsilateral mediastinal shift (indicated by black arrow).

Left upper lobe pneumonia

ACUTE ASTHMA IN CHILDRENS

Clinical features

- Typical features: usually intermittent and can occur either sporadically or in response to an asthma trigger.
- Persistent, dry cough that worsens at night, with exercise, or on exposure to triggers (cold air, allergens, smoke)
- End-expiratory wheezes
- Dyspnea (shortness of breath) and chest tightness, particularly on exertion.
- Prolonged expiratory phase on auscultation
- Hyperresonance to lung percussion
- Features of atopy (e.g., allergic rhinitis, eczema, food allergy).
- In chronic cases: On inspection, look for eczematous skin changes (particularly in the flexures), hyperinflation of the chest and, if a long history, **Harrison's sulcus** – a permanent horizontal groove inferior to the costal margin.
- Life-threatening asthma
 - SpO₂ <92% in air PLUS, any of the following
 - PEFR ≤ 30% best or predicted in aged ≥ 5 years
 - Decreased air entry/silent chest
 - Poor respiratory effort
 - Altered conscious level
 - Cyanosis/pallor

Diagnostic workup

- Pulmonary Function Testing (Spirometry): first-line diagnostic test, perform in children aged over 5 years.
- Chest X-ray: Normal in mild cases
- Allergy testing: CBC (possible eosinophilia), skin allergy tests (skin prick testing), serum IgE level

ASSESSMENT OF ACUTE ASTHMA ATTACK

Clinical features	Mild	Moderate	Severe
Symptoms			
Breathlessness	While walking	While at rest	At rest
Position	Can lie down	Prefers sitting	Hunched over
Ability to speak	Sentences	Phrases	Individual words
Alertness	Maybe agitated	Usually agitated	Agitated
Signs			
Respiratory rate	Increased	Increased	Often >30/minute
Wheezing	Moderate, often only end-expiratory	Loud; throughout exhalation	Throughout inhalation and exhalation; can also be absent
Use of accessory muscles	Rarely	Commonly	Usually
Pulse/minute	<100	100-120	>120
Pulsus paradoxus	Absent	Maybe present	Often present
PCO ₂	<42 mm Hg	>42 mm Hg	≥42 mm Hg
SaO ₂	>95%	90-95%	<90%



TREATMENT OF ACUTE ASTHMA IN CHILDRENS

- Stabilize patient using ABCD&E approach
- Establish intravenous (IV) access
- Vitals monitoring: BP, PR, RR, Temp. & check SpO₂ → Give high flow O₂ as needed, aim to keep SpO₂ 94-98%
- Nebulized SABA: Salbutamol (Ventolin solution) at dose 0.15 mg/kg (minimum 2.5mg/dose) dilute in 2-3ml 0.9% NS, nebulizer every 20 minutes for up to 3 doses, followed by 0.5 mg/kg/hour nebulized continuously or 2.5mg to 10mg every 1-4 hours when needed.
- Nebulized SAMA (If no response or Moderate to severe asthma): Ipratropium bromide (Atrovent 0.025%/2ml)
 - Children ≤5 years of age: 250 mcg nebulized every 20 minutes for 3 doses; children 6-11 years of age: 250-500mcg nebulized every 20 minutes for 3 doses.
- Give Inj. Hydrocortisone 100mg/vial (Solu-cortif) at dose 4mg/kg/dose x IV STAT (Maximum: 100mg/dose)
- Avoid triggers: This process may be initiated by a large number of allergens – classically cold air, exercise, viral or bacterial infections, pollen, animal dander, dust mites, emotion, medication and cigarette smoke

STATUS ASTHMATICUS IN CHILDREN

Clinical examination

Features of severe asthma

- » Wheezing
- » Accessory muscle usage
- » Paradoxical breathing
- » Decreased breath sounds
- » Prolonged expiratory phase
- » Tachypnea
- » Pulsus paradoxus
- » Hyperresonance

- » **Auscultation** (Characteristic findings are usually only present during acute attacks)
 - Prolonged expiratory phase with wheezing (dry crackles)
 - Decreased breath sounds; possibly "silent chest"
 - Tachypnea
- » **Percussion:** Hyperresonant sound, Inferior displacement & poor movement of the diaphragm
- » **In severe attacks:** ALOC, Cyanosis

Rx

☞ Stabilize patient using ABCD&E approach

☞ Establish intravenous (IV) access

☞ **Vitals monitoring:** BP, PR, RR, temp. and check SpO₂ & Give high flow O₂ as needed, aim to keep SpO₂ 94-98%

☞ **Noninvasive ventilation (NIV):** BiPAP provides greater support, maintains airways open → decreases airways resistance → reduces auto-PEEP → reduces work of breathing, use for 1-2 hours in cooperative patients not responding to medical therapy.

☞ **Obtain investigation:** CBC, serum IgE, ABGs and PFTs (spirometry)

☞ **Nebulized SABA: Salbutamol** (Ventolin solution) at dose 0.15 mg/kg (minimum 2.5mg/dose) dilute in 2-3ml 0.9% NS, nebulizer every 20 minutes for up to 3 doses, followed by 0.5 mg/kg/hour nebulized continuously or 2.5mg to 10mg every 1-4 hours when needed.

☞ **Nebulized SAMA: Ipratropium bromide** (Atrovent 0.025%/2ml) x Children ≤5 years of age: 250 mcg nebulized every 20 minutes for 3 doses; children 6-11 years of age: 250-500mcg nebulized every 20 minutes for 3 doses. **Reassess:** if symptoms improve continuous nebulized salbutamol and repeat ipratropium bromide. If poor response, give every 20-30 minute for first 2 hour.

☞ **Corticosteroids: Inj. Dexamethasone 4mg/ml** (Decadron) at dose 0.6 mg/kg orally/intramuscularly/intravenously once daily

OR Inj. **Methylprednisolone sodium succinate 500mg/vial** (Solu-Medrol) at dose 1mg/kg/dose x IV every 6 hrs.

OR Tab. **Prednisolone 5mg** (Deltacortril) at dose 1-2mg/kg/day x orally

Is patient still not improving and meets severe/life-threatening criteria? If YES than start IV SABA (Salbutamol)

☞ Inj. **Salbutamol 0.5mg/ml** (Ventolin) x 1mg (2 ampule) in 100ml 0.9% NS or 5% Dextrose = (10mcg)

Formula: $1\text{mg} \div 100\text{ml} = 0.01 \times 1000 = 10\text{mcg}$

Loading dose: 7.5 mcg/kg over 3-5 minute followed by 1mcg/kg/minute (**Maximum:** 5mcg/kg/minute)

☞ Inj. **Magnesium sulphate** at dosage children ≥2 years of age: 40-50 mg/kg IV by slow infusion, dilute in 100ml 0.9% normal saline over 20-60 minutes, maximum 2000 mg/dose OR Nebulized magnesium sulphate in children ≥2 years of age: 150 mg nebulized every 20 minutes for 3 doses

CHILD WITH COLD/FLU

△

C/C:

- » Fever
- » Sneezing
- » Cough
- » Nasal Discharge
- » Watery eyes

Rx

1. **Syp. Loratidine 5mg/5ml** (Softin, Lorin-NSA)
OR **Syp. Cetirizine 5mg/5ml** (Rigix, Zyretic)

Dosage: age 2-5 years = 5mg x OD, age > 5years 5mg x BD

2. For cough/allergy **Syp. Babynol**, OR **Syp. Combinol Junior**
1-2 teaspoonful BD/TDS

For fever/analgesia: (Calpol 6 Plus, Panadol forte = 250mg/5ml)

3. **Syp. Paracetamol** (Calpol = 120mg/5ml, Panadol = 160mg/5 ml)

Dosage: 10-15mg/kg/dose x TDS/QID. (Max: 75 mg/kg/day)

ALLERGIC RHINITIS

Definition: Allergic rhinitis (AR) is an immunoglobulin E (IgE)-mediated inflammatory nasal condition resulting from allergen exposure in a sensitized individual. Allergic rhinitis is a common inflammatory condition of the URTI, characterized by nasal pruritus, sneezing, rhinorrhea, and nasal congestion. Frequently, there is associated palate, throat, ear, and eye itching as well as eye redness, puffiness, and watery discharge.

Etiology: type-I hypersensitivity reaction (an IgE-mediated process)

Risk factor: family history of allergy or atopy, age <20 years, exposure to aeroallergens such as plant pollens (grasses, trees, weeds), molds spores, house dust mites, cockroaches, latex, pollution)

Clinical features

- Recurrent episodes of:** Nasal pruritus, Sneezing, Rhinorrhea, Nasal congestion, Post-nasal drip
- Associated symptoms:** Itching of palate, throat, ear, and itchy eyes, eye redness (conjunctival conjuction), puffiness, and watery discharge.
- Constitutional symptoms:** Fatigue, Irritability.
- Associated allergic conditions:** Allergic conjunctivitis, Atopic dermatitis and/or bronchial asthma
- Physical examination of the nose:** may include swelling of the turbinates and nasal mucosa, the presence of clear nasal mucus and/or a pale nasal mucosa, and nasal crease (a transverse crease resulting from repetitive nose rubbing and manipulation).
- Physical exam of the face:** may identify allergic shiners (bluish discoloration in the infraorbital region), conjunctival injection, ocular mucoid discharge, & less commonly, Dennie-Morgan lines (creases present under the lower eyelids).

CLINICAL CLASSIFICATION OF ALLERGIC RHINITIS

	Classification criteria	Definition
Temporal pattern of allergen exposure	Episodic allergic rhinitis	Symptoms occur on exposure to allergens that are not normally a part of the individual's environment
	Seasonal allergic rhinitis	Symptoms occur on exposure to allergens that occur during particular seasons.
	Perennial allergic rhinitis	Symptoms occur on exposure to allergens that are normally a part of the patient's environment
Frequency	Intermittent allergic rhinitis	Duration of symptoms: < 4 days/week or < 4 weeks/year
	Persistent allergic rhinitis	Duration of symptoms: > 4 days/week for > 4 weeks/year
Severity	Mild allergic rhinitis	Symptoms do not interfere with the quality of life.
	Moderate to severe allergic rhinitis	Symptoms interfere with the quality of life.



TREATMENT OF ALLERGIC RHINITIS

- Allergen avoidance:** advice patient to avoid exposure to allergen is one of the guiding principles of treatment.
- First line treatment – Intranasal steroids:** In patients with mild or intermittent symptoms
 - Fluticasone 50mcg nasal spray (Flixonase or Ticovate) x In children ≥4 years of age at 1-2 sprays (50mcg/spray) in each nostril twice daily
 - OR Mometasone nasal spray (Rinelon or Hivate) x In children ≥2 years of age: 1 spray (50mcg/spray) in each nostril once daily; children ≥12 years of age: 2 sprays (100mcg) in each nostril once daily
- 2nd gen. Antihistamine:**
 - Syp. Loratidine 5mg/5ml (Softin, Lorin NSA)
 - OR Syp. Desloratadine 0.5mg/5ml (Jordin-D, Neo-Initial)
 - OR Syp. Levocetirizine 2.5mg/5ml (T-Day, Neo-sedil, Ocitra)

Treatment duration 5-7 days
- Intranasal antihistamine** are another first-line option when symptoms are intermittent and do not require daily medication. If symptoms are persistent, an intranasal corticosteroid and intranasal antihistamine may be continued in combination.
 - Azelastine 0.1% (=137mcg) nasal spray (Azosin) x In children ≥5 years of age: 1 spray (137mcg/sprays) in each nostril twice daily; children ≥12 years of age: 1-2 sprays (137-274mcg) in each nostril twice daily
 - Olopatadine 0.6% nasal spray (Olonase) x In children ≥6 years of age: 1 spray ((665mcg/spray) in each nostril twice daily; children ≥12 years of age: 2 sprays in each nostril twice daily. **N.B.** Excessive use of nasal drops and sprays should be avoided because it may lead to rhinitis medicamentosa
- Referral to ENT specialists for further management



CHILD WITH DENTAL INFECTION

Name: Age: Sex: Date: Temperature: B.P.: Pulse: Resp. Rate:	△ Dentoalveolar Infections c/c: » Toothache » Fever and sickness » Cheek swelling/swollen gums » Tooth sensitivity to hot, cold or pressure » Swollen lymph nodes » Redness or swelling of the gums next to a tooth. » Loss of appetite » Puss formation Avoid chilled carbonated drinks, chocolates and candies. If your children are young don't allow them to sleep with a milk bottle in their mouth, this way carbohydrate content in the milk reacts with acids in saliva and starts eating the tooth enamel and this leads to tooth decay. Duration of antibiotics: 4-7 days
Rx 156.25mg/5ml (Augmentin, Calamox) 1. Syp. Co-Amoxiclavate 312.50mg/5ml (Augmentin DS, Calamox DS) Dosage: 25-40mg/kg/day x divided every 8-12 hourly. TDS/BD (1 Teaspoonful = 5ml) OR Syp. Cefadroxil 125mg/5ml, 250mg/5ml (Cedrox, Durcel) Dosage: 30mg/kg/day divided every 12 hourly PO (Max: 2g/day). BD (1 Teaspoonful = 5ml) For fever/analgesia: (Calpol 6 Plus, Panadol forte = 250mg/5ml) 2. Syp. Paracetamol (Calpol = 120mg/5ml, Panadol = 160mg/5 ml) Dosage: 10 – 15mg/kg/dose x TDS/QID. Maximum 75 mg/kg/day OR Syp. Ibuprofen (Brufen = 100mg/5ml, Brufen DS = 200mg/5ml) Dosage: 10mg/kg/dose x TDS/QID Maximum daily dose: 40mg/kg/day ± For reduced gum swelling and abscess 3. Syp. Metronidazole 200mg/5ml (Flagyl, Klint, Metrozine) Dosage: 7.5 mg/kg/dose three times a day TDS (1 Teaspoonful = 5ml)	

CHILD WITH EAR PAIN

Name:	Age:	Sex:	Date:
Temperature:	B.P.	Pulse:	Resp. Rate:
△ c/c: » Ear pain/Otalgia » Irritability » Incessant crying » Refusal to feed » Fever sometime	Rx 1. Lidocaine Ear drops (Otocain, Lidosporin) 2-3-drops 3-4 time a day For pain/analgesia: (Calpol 6 Plus, Panadol forte = 250mg/5ml) 2. Syp. Paracetamol (Calpol = 120mg/5ml, Panadol = 160mg/5 ml) Dosage: 10 – 15mg/kg/dose x TDS/QID. Maximum 75 mg/kg/day OR Syp. Ibuprofen (Brufen = 100mg/5ml, Brufen DS = 200mg/5ml) Dosage: 10mg/kg/dose x TDS/QID (Maximum dose: 40mg/kg/day)		

CHILD WITH EAR DISCHARGE/INFECTION

Clinical features

Ear pain: Older children will most frequently report ear pain; in infants and nonverbal children's symptoms can be nonspecific and may be easily confused with other conditions.

General symptoms

» Otalgia/earache, commonly described as throbbing pain

» Hearing loss in the affected ear

» Fever

» Otorrhea (Ear discharge) in the case of a ruptured tympanic membrane

Typical presentation in infants

» Irritability, Incessant crying

» Refusal to feed (anorexia)

» Repeatedly touching the affected ear

» Fever and febrile seizures

» Vomiting, fever and febrile seizures

» Duration of Antibiotics: 5-7 days

Rx

156.25mg/5ml (Augmentin, Calamox)

1. Syp. Co-Amoxiclave 312.50mg/5ml (Augmentin DS, Calamox DS)
Dosage: 25-40mg/kg/day x divided every 8-12 hourly.
 TDS/BD (1 Teaspoonful = 5ml)
 OR Syp. Cefadroxil 125mg/5ml, 250mg/5ml (Cedrox, Duricef)
Dosage: 30mg/kg/day divided every 12 hourly PO (Max: 2g/day).
 Twice daily (BD) according to body weight (1 Teaspoonful = 5ml)

For fever/pain/analgesia:

(Calpol 6 Plus, Panadol forte = 250mg/5ml)

2. Syp. Paracetamol (Calpol = 120mg/5ml, Panadol = 160mg/5 ml)
Dosage: 10 – 15mg/kg/dose x TDS/QID. Maximum 75 mg/kg/day
 OR Syp. Ibuprofen (Brufen= 100mg/5ml, Brufen DS= 200mg/5ml)
Dosage: 10mg/kg/dose x TDS/QID (Max dose: 40mg/kg/day)
3. Ciprofloxacin + Lidocaine Ear drops (Cipocain)
 OR Ciprofloxacin + Lidocaine Ear drops (Cipocain)
 2-3-drops 3-4 time a day



DENTAL INFECTIONS IN CHILDREN

1. Pain, fever and Symptom Management

(Calpol 6 Plus, Panadol forte = 250mg/5ml)

- » Syp. Paracetamol (Calpol = 120mg/5ml, Panadol = 160mg/5 ml)
Dosage: 10 – 15mg/kg/dose x TDS/QID. Maximum 75 mg/kg/day
 - » OR Syp. Ibuprofen (Brufen= 100mg/5ml, Brufen DS= 200mg/5ml)
Dosage: 10mg/kg/dose x TDS/QID (Max dose: 40mg/kg/day)
2. Antibiotic Therapy: Indications include Systemic involvement, spreading infection, or inability to access immediate dental care. 156.25mg/5ml (Augmentin, Calamox)
- » Syp. Co-Amoxiclave 312.50mg/5ml (Augmentin DS, Calamox DS)
Dosage: 25-40mg/kg/day x divided every 8-12 hourly.
 TDS/BD (1 Teaspoonful = 5ml)
 - » OR Syp. Cefadroxil 125mg/5ml, 250mg/5ml (Cedrox, Duricef)
Dosage: 30mg/kg/day divided every 12 hourly PO (Max: 2g/day).
 Twice daily (BD) according to body weight (1 Teaspoonful = 5ml)
 - » Clindamycin (for penicillin-allergic patients): 8-20 mg/kg/day divided every 6-8 hours for 7-10 days.
3. Drainage of Abscess
- » Incision and Drainage: Performed by a dentist or oral surgeon if an abscess is present.
 - » Pulpotomy or Pulpectomy: For abscessed primary teeth to remove the infected pulp tissue.
4. Definitive Dental Treatment
- » Restorative Procedures:
 - Fillings: For small cavities to restore the tooth.
 - Crowns: For extensive decay or after pulpotomy/pulpectomy.
 - » Extraction: If the tooth is severely decayed or the infection cannot be resolved with conservative treatment.

ACUTE SUPPURATIVE OTITIS MEDIA (ASOM)



- » Acute inflammation of middle ear cleft <3 weeks, infective in origin.
- » One of the most common infectious diseases seen in children
- » **Peak incidence** - first 2 years of life
- » **Most common route of infection** is through Eustachian tube
- » **Organism**
 - » **Bacterial:** Streptococcus pneumoniae (Most common), H. influenzae (2nd most common), Moraxella catarrhalis
 - » **Viral:** Syncytial virus, Influenza virus, Rhino and adeno virus

Stages of ASOM

1. Stage of tubal occlusion
2. Stage of pre-suppurative
3. Stage of suppuration
4. Stage of resolution
5. Stage of complication

△ ASOM

C/C:

- » **Ear Pain:** Older children will most frequently report ear pain; in infants and nonverbal children's symptoms can be nonspecific and may be easily confused with other conditions.
- » **General symptoms**
 - Otalgia/Earache commonly described as throbbing pain.
 - Hearing loss in the affected ear
 - Fever
 - Otorrhea (Ear Discharge) in the case of a ruptured tympanic membrane.

Examination findings**Otoscopy**

- » Bulging tympanic membrane (TM) with loss of landmarks
- » Opacification and loss of light reflex
- » Retracted and hypomobile TM
- » Purulent/serosanguinous discharge in the external auditory canal or visible perforation
- » Distinct erythema of the TM
- » **Additional findings that may be present:** Yellow spot on the TM, Cartwheel TM, Blisters/bullae on the Tympanic membrane (TM)

Tuning fork test: hearing loss secondary to an effusion.

CBC: Leukocytosis maybe present

Gram stain and culture of middle ear fluid - if patient not responded to Rx

Blood cultures: indicated only in severe infection

Duration of antibiotics: 7-10 days

Rx

1. **Syp. Amoxicillin 125mg/5ml, 250mg/5ml** (Amoxil, Zeemox)
Dosage: 40mg/kg/day in three divided doses
TDS (1 Teaspoonful = 5ml)

312.50mg/5ml (Augmentin DS, Calamox DS)

OR **Syp. Co-Amoxiclave 156.25mg/5ml** (Augmentin, Calamox)

Dosage: 25-40mg/kg/day x divided every 8-12 hourly.

TDS/BD (1 Teaspoonful = 5ml)

For fever/analgesia: (Calpol 6 Plus, Panadol forte = 250mg/5ml)

2. **Syp. Paracetamol** (Calpol = 120mg/5ml, Panadol = 160mg/5ml)

Dosage: 10 - 15mg/kg/dose x TDS/QID. Maximum 75 mg/kg/day

OR **Syp. Ibuprofen** (Brufen = 100mg/5ml, Brufen DS = 200mg/5ml)

Dosage: 10mg/kg/dose x TDS/QID (Max dose: 40mg/kg/day)

3. **Polymyxin + Lidocaine Ear drops** (Otocain)

OR **Ciprofloxacin + Lidocaine Ear drops** (Cipocain)

2-3-drops 3-4 time a day

Rx

1. **Syp. Cefaclor 125mg/5ml, 250mg/5ml** (Ceclo, Cefalor)

Dosage: 20mg/kg/day 2-3 times a day
BD/TDS (1 Teaspoonful = 5ml)

(Cefspan DS, Cefiget DS = 200mg/5ml)

OR **Syp. Cefixime** (Cefspan, Cefiget = 100mg/5ml)

Dosage: 16mg/kg/day every 12 hourly on day 1, then 8 mg/kg/day for 13 days.

BD (1 Teaspoonful = 5ml)

(Ponstan DS 100mg/5ml, Dollar DS 100mg/5ml)

2. **Syp. Mefenamic acid** (Ponstan 50mg/5ml, Dollar 50mg/5ml)

Dosage: 3mg/kg/dose OR in some Books >6 months 6.5-25 mg/kg daily 3-4 times daily for not longer than 7 days.

TDS (1 Teaspoonful = 5ml)

3. **Tobramycin + Dexamethasone Ear drops** (Dexatob)

OR **Ciprofloxacin + Dexamethasone Ear drops** (Cipotec-D)

2-3-drops 3-4 time a day

MANAGEMENT OF FEVER

SYMPTOMS & SIGNS OF SPECIFIC DISEASES

Meningococcal disease

- Non-blanching rash with ≥ 1 of the following:
 1. Ill-looking child
 2. Lesions > 2 mm in diameter (purpura)
 3. Capillary refill time ≥ 3 seconds
 4. Neck stiffness

Meningitis

- Neck stiffness
- Bulging fontanelle
- Decreased level of consciousness
- Convulsive

Herpes simplex encephalitis

- Focal neurological signs
- Focal seizures
- Decreased level of consciousness

Pneumonia

- Tachypnoea, measured as:
 - » Aged < 1 year: R/R ≥ 50 breaths/min
 - » Aged > 1 year: R/R > 40 breaths/min
- Crackles in the chest
- Nasal flaring
- Chest indrawing
- Cyanosis
- SpO₂ $\leq 95\%$

Urinary tract infection

- Vomiting (in children aged > 3 months)
- Poor feeding
- Lethargy
- Irritability
- Abdominal pain or tenderness
- Urinary frequency or dysuria
- Offensive urine or haematuria

Septic arthritis/osteomyelitis

- Swelling of a limb or joint
- Not using an extremity
- Non-weight bearing

Kawasaki disease: Fever lasting > 5 days and ≥ 4 of the following:

- Bilateral conjunctival injection
- Change in upper respiratory tract mucous membranes (e.g. Injected pharynx, dry cracked lips or strawberry tongue)
- Change in peripheral extremities (e.g. Oedema, erythema or desquamation)
- Polymorphous rash
- Cervical lymphadenopathy

Reassure parents with anxiety about the child's fever.

- Explain the nature of the child's illness.
- Fever is not an illness, but a beneficial response of the body to illness. Most fevers are of short duration and are not harmful.
- Children with fever are not at increased risk of seizures, dehydration, brain damage or death.
- Body temperature during fever normally fluctuates and the fever will run its course.
- The fever will return until the illness is better and strict control of fever is never required.
- Tepid sponging not recommended
- Dress child normally
- Either Paracetamol or ibuprofen (not both) can be used to make the child more comfortable.
- Do not routinely administer both drugs at the same time with the sole aim of reducing fever or preventing febrile seizures
- Paracetamol suppositories may be useful when the child is unable to take oral medication.

ANTIBIOTICS

- Do not prescribe oral antibiotics to children with fever without apparent source. If an antibiotic is not indicated, explain the reasons why and harms associated with prescribing an antibiotic.
- If aged > 3 months, consider admission and observation with/without investigations

SIGNS OF SHOCK

- Increased respiratory and heart rate, cold peripheries, prolonged CRT, pallor/mottled, drowsy/agitated/confused
- Give immediate IV fluid bolus of sodium chloride 0.9% 20 mL/kg. Give additional boluses as necessary
- If signs of shock, SpO₂ $< 92\%$ or clinically indicated, prescribe oxygen
- Urgent senior RMO/Consultant support

Antipyretic dosage for infants and children older than 3 months of age:

	Oral dose	Dose frequency	Maximum daily dose
Paracetamol	15mg/kg	6 hourly	90mg/kg
Ibuprofen	10mg/kg	6 hourly	40mg/kg



Base line investigation to rule out the cause

- Complete blood count:
 - » Hb↓, MCV↓ (Iron deficiency Anemia)
 - » Hb↓, MCV↑ (Megaloblastic Anemia)
 - » White blood cells: Inflammation
 - » Neutrophils: Bacterial infection
 - » Lymphocytes: Viral infection
 - » Basophils: Allergic condition
 - » Eosinophils: Parasitic infection
 - » Platelets: Low → thrombocytopenia
- Blood culture and sensitivity (specific cause)
- CRP (C-reactive protein)
- Urine testing for urinary tract infection
- Chest X-ray only if respiratory signs positive
- Stool culture, if diarrhoea is present

Paracetamol Brand Name

- » Inj. Provas 1g/100ml (10mg/ml)
- » Inj. Bofalgan 1g/100ml (10mg/ml)

Intravenous (IV) antipyretics

IV dosage: Paracetamol 15 mg/kg IV infusion (maximum dose 60 mg/kg per 24 hours).

Preparation: 10mg per ml, give undiluted

Syringe: use syringe/infusion according dose, 10ml

BODY WEIGHT	ML	BODY WEIGHT	ML
2kg	3ml	14kg	21ml
3kg	4.5ml	16kg	24ml
4kg	6ml	18kg	27ml
5kg	7.5ml	20kg	30ml
6kg	9ml	22kg	33ml
7kg	11ml	24kg	36ml
8kg	12ml	28kg	42ml
9kg	14ml	32kg	48ml
10kg	15ml	36kg	54ml
11kg	17ml	42kg	63ml
12kg	18ml	48kg	72ml

Advice for parents (and caregivers) about management of fever at home

Do	Don't
Do encourage the child to drink fluids regularly (breast milk is best for breast feeding children).	Don't apply tepid sponging. Sponging the skin with cool water may briefly reduce the temperature of skin being sponged, but it does not reduce inflammation or affect the cause of fever and therefore has no significant lasting effect on body temperature.
Do administer antipyretic medication if the child is distressed.	Don't over-dress or under-dress the child, or wrap the child in heavy blankets.
Do make sure the dose is correct based on the weight of the child.	Don't exceed the maximum recommended doses of antipyretic medication per 24 h.
Do shake the bottle before pouring medicine.	Don't measure medicine using a household teaspoon or tablespoon – use only the measuring device provided.
Do use a syringe or medicine measure spoon to administer medicines.	Don't allow children to drink medicines straight from the bottle.
Do store all medicines out of the reach of children.	Don't administer another dose of antipyretic medication immediately if the temperature does not come down after one dose. Wait for the appropriate dosing interval to pass and only give another dose at the correct time.
Do store all medicines according to the manufacturer's instructions and below 25 °C, out of direct sunlight, with the cap tightly closed. Do not keep medicines in the car or bathroom cabinet.	Don't wake a sleeping child just to administer antipyretic medication.
Do seek further medical advice if the fever does not get better within 48 h, or if the child's condition gets worse	Don't give antipyretic medicine to the child for longer than 2 days without consulting a doctor.
	Don't give a child antipyretic medication before or immediately after vaccination.

✓ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3063696/>

✓ Nice guidelines, BNF, guidelines – UK

ENTERIC FEVER (TYPHOID FEVER)

Clinical features

- Incubation period: 5–30 days (most commonly 7–14 days)
- Fever that rises gradually low to 39°C to 40°C (102°F to 104°F), height of fever usually occurring in the afternoon.
- Dull frontal headache
- Nausea/Vomiting
- Malaise, weakness, tiredness
- White Coated tongue
- Relative bradycardia
- Loss of appetite
- Abdominal pain
- Rose color spots: erythematous maculopapular rashes, usually 2–4 mm on chest, back & abdomen
- Diarrhea or constipation
- Hepatosplenomegaly may exist

Diagnostic workup

- CBC: mild anemia, Leukopenia or leukocytosis (may suggest perforation or suppuration), platelets – low to normal
- LFTs: Maybe mild abnormal
- Test of choice: **Blood culture**
- The most important diagnostic test at disease onset, as stool culture are often negative despite active infection. Stool culture often positive after 1 week of infection. Urine culture has low sensitivity.
- Gold standard test
- Bone marrow culture
- Ultrasound abdomen:
- Hepatosplenomegaly

N.B. The following test are no longer recommended because of low sensitivity: Typhidot-M, Widal test, IDL Tubex test.

Rose colored spots



Treatment duration: 7–14 days

Prevention: Salmonella infection is best prevented by protecting the water supply, preventing fecal contamination during food production, cooking and refrigerating foods, pasteurizing milk and milk products, and handwashing before preparing foods and vaccination (To date, 3 types of typhoid vaccines exist)

Rx

OPD (Outpatient) treatment for mild to moderate (Cefspan DS, Cefiget DS = 200mg/5ml)

- Syp. Cefixime 100mg OR 200mg (Cefspan, Cefiget = 100mg/5ml)
Dosage: 15–20 mg/kg/day orally given in 2 divided (BD) doses.
 OR Syp. Ciprofloxacin 125mg OR 250mg (Novidat, Mytil)
Dosage: 15–30 mg/kg/day x BD (Maximum dose: 1500 mg/day)
 OR Syp. Azithromycin 200mg/5ml (Zetro, Azomax, Azitma)
Dosage: 8–10 mg/kg/day x OD for 7–10 days
 (Calpol 6Plus, Panadol forte = 250mg/5ml)
- Syp. Paracetamol (Calpol = 120mg/5ml, Panadol = 160mg/5 ml)
Dosage: 10–15 mg/kg/dose x TDS/QID
 OR Syp. Ibuprofen (Brufen = 100mg/5ml, Brufen DS = 200mg/5ml)
Dosage: 10 mg/kg/dose x 6 to 8 hourly (TDS/QID).
Maximum dose: 40 mg/kg/day
- Syp. Multivitamins/appetite stimulant (Lysovit, Tresorix forte)
 5–10 ml once or twice daily (OD/BD)

Rx

Hospital (inpatient) treatment for severe/complicated

- Stabilize patient using ABCD&E approach
- Establish intravenous (IV) access
- Vitals monitoring: BP, PR, RR, Temperature, SpO₂
- Obtain CBC, LFTs, RBS, blood culture (before antibiotics) and US abdomen
- IV hydration: Patients often require supportive care with IV fluid
 - Inj. Ringer Lactate OR Inj. 0.9% Normal saline x IV x OD
 - Dose: 20ml/kg IV fluid bolus
- Inj. Ceftriaxone 1g (Oxidil, Rocephin) at dose 50–75mg/kg/day x IV x BD/OD
Alternative:
 - Inj. Cefotaxime 1g/vial (Claforan, Cefotax) at dose 40–80 mg/kg/day x in 2 to 3 divided doses (BD/TDS)
 - Inj. Cefoperazone 1g/vial (Cefobid) at dose 50–100 mg/kg/day x BD
 - Inj. Ciprofloxacin 200mg/100ml (Ciplet, Novidat) x IV x BD
Dosage: 15 mg/kg/day (Maximum: 20 mg/kg/day)
 - Inj. Azithromycin 500mg (Azitma, Zetot) in 100ml 0.9% NS x IV x OD
Dosage: 8–10 mg/kg/day, (In drug resistant: 10–20 mg/kg/day)
- For fever: Inj. Paracetamol 1g/100ml (Provas, Bofalgan, Otsumol) at dose 10–15mg/kg/dose IV x TDS
- For vomiting: Inj. Dimenhydrinate 50mg/1ml (Gravinate) at dose 0.5–1mg/kg/dose x IV x TDS, if not response than Inj. Ondansetron 8mg/4ml (Onset, Onseron) x at dose 0.15 mg/kg/dose over 15 min is given by IV infusion diluted in 25 to 30ml of 0.9% NS OR D5%W
- For severe: Inj. Dexamethasone 4mg/1ml (Decadron) initially 3 mg/kg x IV followed by at doses 0.6 mg to 1 mg/kg x every 6 hours for 48 hours.



Clinical features

- » Fever or H/O fever, Chills & rigors (= shivering and feeling very cold)
- » Associated with Sweats, tachycardia
- » General malaise, weakness
- » Headache, myalgia, arthralgia
- » Abdominal pain, diarrhea
- » Nausea and vomiting.
- » Loss of appetite
- » Jaundice
- » Alter level of consciousness
- » Seizures
- » Anuria, oliguria
- » Hepato-splenomegaly

Diagnostic workup

- » **Test of choice:** Giemsa-stained thick and thin blood smears → detection of asexual or sexual forms of the parasites inside erythrocytes.
- » Rapid Malaria ICT (not recommended)
- » **CBC:** mild anemia, Low platelets, WBCs may be high, low, or normal.
- » **PT:** may be moderately prolonged.
- » **Urea, Creatinine & Electrolytes:** usually normal or mildly impaired; acute renal failure may be present in severe infection
- » **LFTs:** maybe abnormal
- » **RBS:** Hypo- or hyper-glycemia
- » **Urinalysis:** maybe abnormal

Treat malaria as falciparum until proven other wise

MALARIA FEVER

Rx Treatment of Plasmodium falciparum malaria: uncomplicated disease

P. falciparum malaria originating in chloroquine-sensitive region

- » Chloroquine phosphate (Tab. Nivaquine-P 250mg, Syp. Nivaquine-P 50mg/5ml) at dose 10mg/kg orally as a single dose initially, followed by 5mg/kg at 6, 24, and 48 hours, total dose 25 mg/kg.

P. falciparum malaria originating in chloroquine-resistant region

- » Syp. Artemether 15mg + Lumefantrine 90mg (15+90mg/5ml) Once or twice daily (See standard dosage below chart)

Suspension brands: Syp. Artem, Syp. Artheget junior, Syp. Gen-M in preparation 15mg/90mg/5ml in 30ml and 60ml bottle.

- » OR Tab. Artemether 20mg + Lumefantrine 120mg

➤ **Drug brands:** Tab. Artem 20/120, Tab. Gen-M 20/120

➤ **Dosage for Children:** (20/120mg tablet) 1 dose initially followed by another dose at 8 hours than 1 dose twice daily for 2 days, total 6 doses.

Children 5-15 kg: 1 tablet per dose

Children 15-24 kg: 2 tablets per dose

Children 25-34 kg: 3 tablets per dose

Children ≥ 35 kg: 4 tablets per dose

For fever/analgesia: (Calpol 6Plus, Panadol forte =250mg/5ml)

- » Syp. Paracetamol (Calpol =120mg/5ml, Panadol =160mg/5ml)
Dosage: 15mg/kg/dose every 6 – 8 hours (TDS/QID)

- » OR Syp. Ibuprofen (Brufen = 100mg/5ml, Brufen DS = 200mg/5ml)
Dosage: 10mg/kg/dose x 6 – 8 hourly

Maximum daily dose: 40mg/kg/day x TDS/QID

For generalize weakness/anorexia

- » Syp Multivitamins/Appetite stimulant (Lysovit, Tresorix forte) 5 – 10 ml once or twice daily (OD/BD)

DOSAGE AND ADMINISTRATION OF ARTEMETHER 15MG + LUMEFANTRINE 90MG ORAL SUSPENSION

Body Weight (Kg)	1 st Day	2 nd Day	3 rd Day
5 – 7.4 Kg	7 ml	7 ml	7 ml
7.5 – 9.9 Kg	10 ml	10 ml	10 ml
10 – 12.4 Kg	14 ml	14 ml	14 ml
12.5 – 14.9 Kg	17 ml	17 ml	17 ml
15 – 17.4 Kg	20 ml	20 ml	20 ml
17.5 – 19.9	24 ml	24 ml	24 ml
19.9 – 25 Kg	26 ml	26 ml	26 ml

Note:

- » Daily dosage for 3 days x once or twice (OD/BD), should be taken with food or milk.
- » Patients who vomit within 1 hour of taking the medication should repeat the dose.

CHILDHOOD TUBERCULOSIS (TB)

Age:

Sex:

Date:

B.P:

Pulse:

Resp. Rate:

Clinical Manifestation

Tuberculosis (TB in Urdu = تَب دِق), usually presents with a slow onset illness. Adolescents and some older children present in a similar way to adults, while younger children often have non-specific symptoms and signs. Ask and look for the following TB signs and symptoms and decide accordingly:

- » Chest
 - » Cough > 2 weeks (unremitting and not improving)
 - » Sputum
 - » Shortness of breath
 - » Unilateral wheeze, dullness
- » Systemic
 - » Fever > 2 weeks, low grade (99° F)
 - » Sweating at night
 - » Malnutrition or failure to gain weight (Protein Caloric Malnutrition – Grade-3), has not responded to 1 month dietary plan
 - » Low immune status: H/O pertussis or measles (in last 6 months)
 - » Lymph nodes: Cervical lymph nodes (enlarged, painless, matted, or there is an abscess with or without discharge)
 - » BCG scar absent
- » Meningitis
 - » Headache, vomiting
 - » Irritability, lethargic
 - » Neck stiffness
 - » Bulging anterior fontanelle
 - » Coma
- » Abdomen
 - » Chronic diarrhea
 - » Distended abdomen
 - » Any mass, or ascites
- » Bones and joints
 - » Backache, stiffness
 - » Lump, deformity, limp
 - » Unilateral swelling of joint
 - » Any tenderness (slow onset)

PPA SCORING CHART

Scoring chart for the diagnosis of childhood tuberculosis (<15 years) recommended by the Pakistan Paediatric Association (PPA) and National TB programme Pakistan.

Condition	Scores				
	1	2	3	4	5
Age	<5 years				
Close contact	TB suggestive	B-ve, Clinically positive	Bacteriological positive (B+ve)		
Protein Energy Malnutrition (PEM)/Severe acute malnutrition(SAM)	Yes	Not responding to Nutritional rehab for 02 months			
H/O Measles, Whooping Cough	3-6 months	<3 months			
HIV		Yes			
Immunocompromised	Yes				
Clinical Manifestation		Suggestive of TB		Strongly suggestive of TB	
Radiological Imaging	Non-specific	Suggestive of TB	Strongly suggestive of TB		
Tuberculin skin test	5 – 10 mm		> 10 mm		Positive for TB
Gene-Xpert MTB/RIF					Positive for TB
Microscope examination of tissue (Granuloma)	Non-specific				

INTERPRETATIONS - PPA SCORING CHART

Interpretation of Pakistan Paediatric Association (PPA) scores for the diagnosis of childhood tuberculosis (<15 years).		
Score	Interpretation	Suggested Actions
0 – 2	Unlikely TB	Investigate other reasons of illness
3 – 4	Possible TB	Do not treat for TB, Manage the presenting symptom(s)
5 – 6	Possible TB	Monitor monthly the condition(s) for 3 months
7 or above	Probable TB	Investigate and exclude other causes of illness, Investigation may justify therapy
		Confirm (if possible)

EVALUATION OF PRESUMPTIVE TB IN CHILDREN'S

- Identify presumptive TB in children's**
- Every child <15 years should be assessed for presumptive TB if he/she presents with:
 - "Prolonged or Unexplained illness of >2 weeks" With one or >1 the following:
 - Cough > 2 weeks (or uncertain duration)
 - Fever (usually low grade at evening)
 - Enlarged cervical lymph nodes
 - Failure to thrive/weight loss
 - History of known contact of pulmonary TB patient (Bacteriologically positive)
 - HIV infected child/immune compromised
 - Meningitis
 - Most of the patient with childhood TB can be diagnosed on the basis of
 - Close contact history
 - Clinical signs and symptoms
 - Supportive investigations
 - Interpretation of PPA Scoring Chart

Evaluation of presumptive TB in children: Detailed history, clinical examination and interpretations of PPA scoring chart

Findings	Action
If severely ill	» Refer to child specialist
If possible, case of TB, Investigations	» Bacteriological confirmation: » AFB smear microscopy » Gene-Xpert » Culture & sensitivity » Tuberculin skin test (TST)
	» X-ray chest PA view
	» Non-specific: Serology, ESR (Not recommended)
If well	» If age < 5 years give INH prophylaxis
	» If age > 5 years keep under observation

Diagnosis:

- Decide on findings of clinical examination & investigation results
 - If any specimen found bacteriologically positive, declare and manage TB.
 - In cases where the child is not found bacteriological positive, the PPA Scoring Chart helps in evaluating probable TB on the basis of multiple features described in PPA scoring chart

TREATMENT OF TUBERCULOSIS (TB) – Notifiable disease

- Counsel the parents/attendant:** TB is curable, its diagnosis and treatment is free in Pakistan, Symptoms should improve, if not improving come back, Stress importance of DOT, daily treatment and supervision by parent, Ask to bring the other under five children with similar signs to the TB Care Facility, Direct observation and support by parent and selected Treatment supporter, Identify household contacts for further management. Good nutrition is essential for the child including breast feeding (if child is breast fed)
- Ask and record full address of patient & contact person details, fill TB registration form – extremely important
- Discuss treatment with local TB team and lead paediatrician for TB
- Complete clinical and prescription details on patient TB Treatment Card & follow-up visit: 2nd, 5th and 6th Month
- Recommended daily doses of first line ATT:

Anti-TB drugs	Dose in mg/kg/day	Maximum dose
Isoniazid (H)	10mg/kg/day (7 – 15 mg)	300 mg/day
Rifampicin (R)	15 mg/kg/day (10 – 20 mg)	600 mg/day
Pyrazinamide (Z)	35mg/kg/day (30 – 40 mg)	
Ethambutol (E)	20mg/kg/day (15 – 25 mg)	

The tubercle bacilli are killed only when anti TB drugs are given in correct dosage and duration. Irregular treatment leads to resistance and for the proper absorption of anti-TB drugs taking them empty stomach should be preferred

- Available drug brand: H 50mg + R 75mg + Z 150mg (Tab. Rifazol Pediatric)
- Available drug brand: H 50mg + R 75mg + Z 150mg + E 100mg
- Available drug brand: H 50mg + R 75mg

RECOMMENDED TREATMENT REGIMENS FOR TB IN CHILDREN'S

TB Diagnostic category	ANTI-TB DRUGS REGIMENS	
	Intensive phase	Continuation phase
Low HIV prevalence (and HIV-negative children) and low isoniazid resistance settings		
• Smear negative pulmonary TB	2 HRZ	4 HR
• Intrathoracic lymph node TB		
• Tuberculosis peripheral lymphadenitis		
• Extensive pulmonary disease	2 HRZ + E	4 HR
• Smear-positive pulmonary TB		
• Severe forms of extra-pulmonary TB (other than TB meningitis/osteoarticular TB)		
Tuberculous meningitis and osteoarticular TB	2 HRZE	10 HR

WEIGHT BAND/NUMBER OF TABLETS ON DAILY BASIS – According National TB control program Pakistan

Phase/daily	Drugs	Duration	<2 kg	2-2.9kg	3-3.9kg	4-7.9kg	8-11.9kg	12-15.9kg	16-24.9kg
Intensive Phase	HRZ (50/75/150mg)	2 months	1/4	1/2	3/4	1 tab.	2 tab.	3 tab.	4 tab.
	E 100mg	2 months	1/4	1/2	3/4	1 tab.	2 tab.	3 tab.	4 tab.
Continuous Phase	HR (50/75mg)	4 months	1/4	1/2	3/4	1 tab.	2 tab.	3 tab.	4 tab.

CHICKENPOX (VARICELLA)

Age:

Sex:

B.P.:

Pulse:

Date:

Resp. Rate:

Rx

TREATMENT OF CHICKENPOX

General treatment

- Maintain Oral hydration/↑ fluid intake with acyclovir
- Isolation, Children suffering from chickenpox must be restrained from attending the school for 6 days after the appearance of the rash, i.e. until all lesions are converted into crusts/scabs
- Itching may be relieved by systemic antihistaminics and/or local application of calamine lotion, potassium permanganate, and sponge baths with antiseptic detergents.
- Nails must be cut short
- Mouth/perineal regions may be treated by rinses/gargles & saline soaks.
- **Secondary bacterial infections with S. Aureus require appropriate antibiotics:** Co-Amoxiclave or Macrolide (Azithromycin/Clarithromycin)
- Acyclovir claims to accelerate rate of clinical and skin lesion improvement, to reduce number of skin lesions, and to cause speedy defervescence.

1. Syp. Acyclovir 200mg/5ml (Acylex, Aclovir)

QID (1 Teaspoonful = 5ml)

Dosage: 2-16 years = 20mg/kg/Dose 4 times daily for 5 days.**Maximum daily dose:** 800mg

2. Syp. Paracetamol (Calpol = 120mg/5ml, Panadol = 160mg/5ml)

TDS/QID (1 Teaspoonful = 5ml)

Dosage: 10-15mg/kg/dose

3. Syp. Cetirizine 5mg/5ml (Rigix, Zyretec)

OR Syp Loratidine 5mg/5ml (Softin, Lorin-NSA)

Dosage: 2-5 years 5mg OD, >5 years 5mg BD Or 10mg OD**If secondary bacterial infection:** 156.25mg/5ml (Augmentin, Calamox)

4. Syp. Co-Amoxiclave 312.50mg/5ml (Augmentin DS, Calamox DS)

Dosage: 25-40mg/kg/day x divided every 8-12 hourly.

TDS/BD (1 Teaspoonful = 5ml)

OR Syp. Azithromycin 200mg/5ml (Zetro, Azomax, Azitma)

OD (1 Teaspoonful = 5ml)

Dosage: 10mg/kg/day x OD

Chickenpox (Lakra Kakra/१५६१५५)

Incubation period: 2 weeks (11-21 days)

Prodromes

- 1-2 days prior to the onset of exanthem
- Presents with constitutional symptoms (fever, malaise)
- More common with primary infection in adults (less typical in children, in which rash is often the first sign of infection)

Exanthem phase

Duration: ~6 days

Presentation

- Widespread rash starting on the trunk, spreading to the face, scalp, and extremities.
- Simultaneous occurrence of various stages of rash:
Erythematous macules → papules → vesicles filled with a clear fluid on an erythematous base → eruption of vesicles → crusted papules → hypopigmentation of healed lesions
- Severe pruritus
- Fever, headache, and muscle or joint pain.



MUMPS (EPIDEMIC PAROTITIS)

Name: _____ Age: _____ Sex: _____ Date: _____
 Temperature: _____ B.P: _____ Pulse: _____ Resp. Rate: _____



Pathogen: Mumps virus from the Paramyxoviridae family.

Transmission:

- » Humans are the sole host, and the virus is transmitted via airborne droplets.
- » Direct contact with contaminated saliva or respiratory secretions
- » Contaminated fomites

Infectivity: Highly infectious, affected individuals are contagious = 3 days before and up to 9 days after disease onset (when the parotid gland becomes swollen).

Diagnostic workup

Laboratory tests, if available, should be conducted to confirm the suspected cases (especially if presentation is atypical or there is a mumps outbreak).

Pathogen detection

- » Real-time reverse transcriptase PCR (rRT-PCR) on serum or buccal or oral swab
- » Viral culture (e.g., on CSF, throat, urine, or saliva maybe positive for at least 1 weeks)

Serology: Positive serum IgM suggests recent infection and confirms the diagnosis.

CBC (Relative lymphocytosis), serum CRP ↑, serum ESR ↑, and serum Amylase ↑

△ Mumps (Kin Pheerey/کن پھیرے)
 C/C:

Most cases: 5–15 years age group.

Incubation period: 16–18 days.

Prodrome:

- » Duration: 3–4 days.
- » Symptoms: Low-grade fever, malaise, headache

Classic course: inflammation of the salivary glands, particularly parotitis

» Duration of parotitis: at least 2 days (may persist >10 days)

» Symptoms

- May initially present with local tenderness, pain, & earache.
- Unilateral swelling of the salivary gland (lateral cheek and jaw area)
- During the course of disease, both salivary glands are usually swollen.
- Redness in the area of the parotid duct
- Possible protruding ears

» Chronic courses are rare.

Subclinical presentation:

- » Nonspecific or predominantly respiratory symptoms
- » Asymptomatic (in 15–20% of cases)

Rx

Mumps is usually self-limited with a good prognosis.

(Unless complications arise).

Rx is mainly supportive care.

Medication for pain and fever

Isolation and Bedrest

Adequate fluid intake

Avoidance of acidic foods/drinks

Topical application of warm or cold packs to the parotid may also relieve discomfort.

If Orchitis: Support of the inflamed testis with a "bridge," and ice packs make the patient feel more comfortable.



(Calpol 6 Plus, Panadol forte = 250mg/5ml)

1. Syp. Paracetamol (Calpol = 120mg/5ml, Panadol = 160mg/5ml)
 TDS/QID (1 Teaspoonful = 5ml)

Dosage: 10–15mg/kg/Dose

OR Syp. Ibuprofen (Brufen = 100mg/5ml, Brufen DS = 200mg/5ml)

Dosage: 10mg/kg/dose x 6–8 hourly

Maximum daily dose: 40mg/kg/day

TDS/QID (1 Teaspoonful = 5ml)

Prophylaxis

Active immunization is given in the form of MMR at 15–18 months, some experts do not favor vaccination against mumps. They feel that there is no need for its prevention.

Immunization, they argue, may postpone the infection to later age when the disease often runs a severe course.

Passive protection can be given by convalescent γ-globulin in a dose of 2.5 mL (IM) as soon as possible after exposure.

MEASELS (RUBEOLA, Urdu = شیشہ)

Definition: It is a highly infectious disease caused by measles virus, characterized by a maculopapular rash, cough, coryza, conjunctivitis, and a pathognomonic enanthem (Koplik spots) with an incubation period of about 10 days.

Etiology: caused by a spherical RNA virus of the genus Morbillivirus and family Paramyxoviridae.

Clinical features

- Incubation period: 10-14 days
- Prodromal/catarrhal stage: 4-7 days
 - » Coryza, cough, and conjunctivitis
 - » Fever
- Koplik spots: Pathognomonic enanthem of the buccal mucosa → Tiny white or bluish-gray spots on an irregular erythematous background that resemble grains of sand
- Exanthem stage: Duration is 7 days (develops 1-2 days after enanthem)
 - » High fever, Malaise
 - » Generalized lymphadenopathy
 - » Erythematous maculopapular, blanching, partially confluent exanthem
 - Begins behind the ears along the hairline
 - Disseminates to the rest of the body towards the feet (palm and sole involvement is rare)
 - Fades after =5 days of onset, leaving a brown discoloration and desquamation in severely affected areas
- Recovery stage: The cough may persist for another week and may be the last remaining symptom.

Diagnostic workup

- » CBC: ↓ leukocytes, ↓ platelets
- » Serology is gold standard: detection of measles-specific IgM & IgG antibodies.
- » Administration of vitamin-A has been reported to reduce seroconversion in vaccinees and should therefore be avoided at or after immunization.
- » The efficacy of ribavirin administration in severe measles is unproven.

Rx

TREATMENT OF MEASELS

- » Treatment is supportive care: such as Antipyretics, vitamin-A supplementation, and cough suppressants.
- » Bacterial superinfection should be promptly treated with appropriate antimicrobials, but prophylactic antibiotics to prevent superinfection are of no known value and are therefore not recommended.
- » Vitamin-A, supplementation for 2 days, repeat in 4 weeks if eye disease present, has been reported to decrease the severity of measles, reduced morbidity and mortality.

Antibiotics for secondary bacterial infection:

1. Syp. Azithromycin 200mg/5ml (Azomax, Zetro)

Dosage: 10mg/kg on day 1 (Max: 500 mg/day) followed by 5mg/kg/day x Once daily for 5 days (Max: 250 mg/day)
- For fever/analgesia: (Calpol 6 Plus, Panadol forte = 250mg/5ml)
2. Syp. Paracetamol (Calpol = 120mg/5ml, Panadol = 160mg/5ml)

Dosage: 10 – 15mg/kg/dose x TDS/QID. (Max: 75 mg/kg/day)

OR Syp. Ibuprofen (Brufen = 100mg/5ml, Brufen DS = 200mg/5ml)

Dosage: 10mg/kg/dose x TDS/QID (Max dose: 40mg/kg/day)

If symptoms of allergy, hay fever, cough & common cold.

3. Syp Dextromethorphan + Chlorpheniramine + Ephedrine
 - » Syp. Corex-D or Syp. Cofrest x 1 – 2 teaspoonful x TDS
4. Vitamin-A supplementation (A-MAX Drops)
 - » Children <6 months of age: 50,000 units
 - » Children 6-11 months of age: 100,000 units
 - » Children ≥12 months of age: 200,000 units

Administration x per orally once daily for 2 days, repeat in 4 weeks if eye disease present.

Complications

1. Pneumonia – Medium likelihood → short-term
2. Otitis media – Medium likelihood → short-term
3. Encephalitis – Low likelihood → short-term
4. Subacute Sclerosing Panencephalitis (SSPE) – Low (long-term)



SUBACUTE SCLEROSING PANENCEPHALITIS (SSPE)

- Definition:** Subacute sclerosing panencephalitis (SSPE) is a progressive neurological disorder of children and young adults that is characterized by a lethal, generalized, demyelinating inflammation of the central nervous system (CNS). It is a slow and a rare complication due to persistent measles virus infection.
- Epidemiology:** Mainly affects males between 8 and 11 years of age, usually develops ≥ 7 years after measles infection.
- Prognosis:** SSPE leads to death within 1–3 years of diagnosis

CLINICAL FEATURES

- Clinical presentation:** characterized by four clinical stages
- Stage I: Dementia, personality changes
 - Stage II: Epilepsy, myoclonus, autonomic dysfunction
 - Stage III: Decerebration, spasticity, extrapyramidal symptoms
 - Stage IV: Vegetative state, autonomic failure

DIAGNOSTIC APPROACH

- Electroencephalography (EEG):** Paroxysmal delta waves (very slow, 1–3/sec), Periodic sharp and slow wave complexes
- Cerebrospinal fluid (CSF) analysis:** $\uparrow$ anti-measles IgG



TREATMENT OF SUBACUTE SCLEROSING PANENCEPHALITIS (SSPE)

- Currently, there is no cure for SSPE. Most treatments are aimed at symptom reduction
- Prevention in the form of the measles vaccination is the only real "cure" for SSPE.
- Good nursing care is the most important aspect of treatment for SSPE, along with anticonvulsant (Epival) and antispasmodic (Baclofen) drugs when needed.

H. PYLORI INFECTION

Δ H. Pylori Infection
C/C:

- After being infected with H. pylori, the child may have an inflammation of the stomach lining. This is called gastritis. But most people never have symptoms or problems from the infection. When symptoms do occur, they may include belly pain, which can:
- Be a dull, gnawing pain
 - Happen 2 to 3 hours after a meal
 - Come and go for a few days or weeks
 - Occur in the middle of the night when your child's stomach is empty
 - Be eased by eating or taking antacid medicine.
- Other symptoms may include:
- Loss of weight
 - Loss of appetite
 - Swelling or bloating
 - Burning
 - Having an upset stomach
 - Nausea/Vomiting

Recommended first-line treatment for *Helicobacter pylori* infection in children:

1. Amoxicillin OR Metronidazole + Clarithromycin + Proton pump inhibitor (PPI) e.g., Omeprazole, esomeprazole
2. Amoxicillin + Metronidazole + Omeprazole



Clarithromycin based triple therapy (14 days)

1. Tab. Clarithromycin 250mg OR 500mg (Klaricid, Claritek)
Dosage: 7.5–15 mg/kg/day up-to 500mg twice daily
1–0–1 (BD) for 14 days
2. Cap. Amoxicillin 250mg, 500mg (Amoxil, Zeemox)
Dosage: 30–50 mg/kg/day up-to 1g twice daily (BD) for 14 days
OR Tab. Metronidazole 200mg OR 400mg (Metrozine, Flagyl)
Dosage: 20 mg/kg/day up-to 400mg twice daily (BD)
1–0–1 (BD) for 14 days
3. Cap. Omeprazole 20mg (Risek, Ruling)
Dosage: 1 mg/kg/day or 20 mg twice daily for 14 days
1–0–1 (BD) کہتے سے 30 منٹ پہلے



ALTERNATIVE PRESCRIPTION

(Klaricid, Claritek)

1. Syp. Clarithromycin 125mg/5ml OR 250mg/5ml
Dosage: 15mg/kg/day up-to 500mg x twice daily (BD)
1–0–1 (BD)
2. Syp. Amoxicillin 125mg/5ml OR 250mg/5ml (Amoxil, Zeemox)
Dosage: 30–50 mg/kg/day up to 1g (BD)
1–0–1 (BD)
3. Syp. Famotidine 10mg/5ml (Polypep, Peptiban, Reducid)
Dosage: 1 mg up to 2 mg/kg/day (Maximum 80mg/day)
1–0–1 (Two times a day) کہتے سے 30 منٹ پہلے

Treatment Duration: 14 days

URINARY TRACT INFECTION (UTI) IN CHILDREN AND ADOLESCENTS

Definition: UTIs are infections of the bladder, urethra, ureters, or kidneys that are most commonly caused by bacteria, especially *E. coli* (approximately 80%). Infections of the bladder or urethra are called lower UTIs, whereas infections involving the kidneys or ureters are called upper UTIs.

Risk factors: Age <1 years, female sex due to shorter urethra, uncircumcised boys in the first year of life, urinary tract stone, catheter induced or previous UTI, bladder or bowel dysfunction, chronic constipation, vesicoureteral reflux, anatomic abnormalities, previous surgery to the urinary tracts, immunosuppression and diabetes mellitus.



Clinical features

- Fever > 102°F (> 39°C) ± with chills
- Irritability (Neonates & infants)
- Poor feeding (Neonates & infants)
- Suprapubic tenderness
- Abdominal flank pain
- Abdominal pain or tenderness
- Urinary frequency
- Painful urination (Dysuria)
- Ill appearance (Neonates)
- Foul smelling (malodorous) urine
- Darker urine/Frank haematuria
- Frequent urination but very little urine comes out.
- Urgent urination
- New onset urinary incontinence
- Vomiting

Diagnostic workup

- **Urinalysis:** best initial test for all patients
 - Should be performed within 60 minutes of obtaining specimen. First morning voids may be best time for sample.
 - **Finding:**
 - Pyuria: Positive leukocyte esterase, ≥5 WBC/HPF or ≥ 8–10 WBC/mm³
 - &/Or Bacteriuria: positive urinary nitrites
- **Urine culture & sensitivity:**
 - Should be done before antibiotics therapy. It will guide appropriate antibiotic for UTI.
 - In patients with complicated or recurrent urinary tract infections, a urine culture should be obtained prior to initiating antibiotic treatment. False negative results are possible if a culture is obtained after the patient has received antibiotics.
- **Imaging tests (Ultrasound, CT scan)** are general not indicated, may be obtained in severe illness or recurrent UTI or suspected urinary tract obstruction.
- **Blood tests** are not routinely performed, maybe indicated in severe complicated cases (Blood culture, BUN, Creatinine)



Uncomplicated UTI – outpatient (OPD) treatment

Starting empiric antibiotic once culture & urinalysis test sent

- **Syp. Cefixime 100mg/5ml** (Cefim, Cefspan), Dosage in Children ≥ 2 months: 8 mg/kg, orally, OD (max. 400 mg/dose) x 7–14 days
- **OR Syp. Cefuroxime axetil 125mg/5ml** (Zecel) at Dosage Children > 2 months: 20–30 mg/kg/day, orally in divided doses every 12 hours (max. 500 mg/dose) for 7–14 days
- **OR Syp. Cephalexin 125mg/5ml OR 250mg/5ml OR Cap. Cephalexin 250mg** (Ceporex, Keflex) at dose 25–50mg/kg/day x three time a day (TDS) for 7–14 days.
- **OR Syp. Nitrofurantoin 25mg/5ml OR Tab. Nitrofurantoin 100mg** at Dosage: in children ≥ 3 month at dose 1–2 mg/kg once daily at bedtime for 5 days. Avoid in G6PD deficient childrens.

Avoid empiric antibiotic monotherapy with amoxicillin or other penicillins because of resistance.

For fever/analgesia: (Calpol 6 Plus, Panadol forte = 250mg/5ml)

- **Syp. Paracetamol** (Calpol = 120mg/5ml, Panadol = 160mg/5 ml)
Dosage: 10 – 15mg/kg/dose x TDS/QID. Maximum 75 mg/kg/day
- **OR Syp. Ibuprofen** (Brufen = 100mg/5ml, Brufen DS = 200mg/5ml)
Dosage: 10mg/kg/dose x TDS/QID (Max dose: 40mg/kg/day)

Urinary- tonic (Reduce and prevent UTI):

- **Syp. Cran-berry extract** (Cranmax aqua, Lian) x 5ml OD for 1–3 years, 5ml BD for 3–12 years



Complicated UTI – inpatient treatment

- Consider admission for any child that is unable to tolerate oral intake or when the diagnosis is uncertain in a markedly ill child.
- **Star IV antibiotics**
 - **OR Inj. Ceftriaxone 1g/vial** (Oxidil, Rocephin) at dose 50 mg/kg IV once daily (max. 2 g/dose)
 - **OR Inj. cefotaxime 1g** (Claforan) at dose 150 mg/kg/day IV in divided doses every 6–8 hours
 - **OR Inj. Ampicillin 1g/vial** at dose ampicillin 50–400 mg/kg/day IV in divided doses every 6 hours (max. 12 g/day)
- **PLUS, Inj. Gentamicin 40mg/ml** at dose 7.5 mg/kg/day IV in divided doses every 8 hours.
- **For fever/analgesia:** Inj. Paracetamol 1000mg/100ml (Provas) at dose 10 – 15mg/kg/dose x TDS/QID. Maximum 75 mg/kg/day

IRON DEFICIENCY ANEMIA



Clinical features	Diagnostic workup
» Signs and symptoms of anemia: Fatigue, lethargy, Pallor (primarily seen in highly vascularized mucosa, e.g., the conjunctiva) » Cardiac: tachycardia, angina, dyspnea on exertion » Nails: Brittle nails, koilonychia (spoon-shaped nails) » Hair loss, Pica » Dysphagia » Angular cheilitis: inflammation and fissuring of the corners of the mouth. » Atrophic glossitis: erythematous, edematous, painful tongue with loss of tongue papillae (smooth, bald appearance)	» CBC: ↓ Hb, ↓ MCV » Iron studies: – Ferritin level: ↓ – TIBC: ↑ » Ultrasound Abdomen Rx 1. Iron supplementation. Syp. Iberet-500 (Ferrous sulphate + B-Complex) OR Syp. Singobion (Iron + B-Complex) OR Syp. Maltofer (Iron Polymaltose) OR Syp. Malficer-F (Iron Polymaltose + folic acid) Dosage: Age <4 years 5ml x BD, >4 years 10ml x BD

PICA EATING DISORDER

» Pica is an eating disorder characterized by the appetite for and ingestion of non-food items like (e.g., hair, clay, mud, soil, chalk, soap, paper, paint). » Persistent ingestion of nonnutritive substances for > 1 month that is inappropriate for developmental age and not part of culturally or socially normative practice. » Pica poses a risk for parasitic infections, micronutrient deficiency, intestinal obstruction, and heavy metal poisoning. Diagnostic workup » CBC to rule out Iron deficiency anemia. » Calcium level to rule out hypocalcemia. » Zinc level - Zinc deficiency	Rx » First line treatment is cognitive behavioral therapy (CBT) » Nutritional supplementation » Use 5-6 weeks then obtained CBC and Calcium level again 1. Syp. Iron supplementation (Iberet-500, Maltofer) Dosage: Age < 4 years 5ml x BD, > 4 years 10ml x BD 2. Syp. Calcium supplementation (Calcium-P, Calone-D) Dosage: 5 – 10 ml x BD, do not advise iron (Fe), calcium or antacids (Gaviscon, Mucain) at the same time because it will inhibit the absorption of iron. It is best to space doses of these medicines 1 to 2 hours apart. If not responded than second line treatment = SSRIs » Syp. Fluoxetine 20mg/5ml (Rize, Depicap) - OR Syp. Escitalopram 10mg/1ml (Prolexa, Citanew)
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VITAMIN-D DEFICIENCY

Clinical features	
Children's » General muscular aches, Weakness ± delayed motor milestones » Bowed legs » Short stature Adolescents » General muscular aches, Weakness » Long bone pain	Rx Prevention » Increase safe sun exposure » Increase vitamin-D in diet (oily fish) » Increase Ca²⁺ intake (Milk) » Treat the underlying cause » Screen the siblings of affected children + offer prevention advice. 1. Syp. Ossein mineral complex + vitamin-D (Calone-D, Osante-D) OR Syp. Magnesium + Vitamin-D + Zinc (Osteocare, Kal-v, Nucal-2) 1-2 teaspoonful x twice daily 2. Cholecalciferol (vitamin D3) Drops (All-D, D-Max, Miura-D3) Dosage: Each drop contains 400 IU of Cholecalciferol » Infants: 1 drops daily » Children under 4 years: 1-2 drop daily. » Children above 4 years: 2-3 drops daily.
Diagnostic workup	
» Serum vitamin-D: ↓ (<25nmol/L) » Serum calcium: Often normal, maybe ↓ » Serum phosphate: Often normal, maybe ↓ » Serum ALP: Elevated in rickets » Serum PTH: ↑ » X-ray in rickets: splaying and fraying of the metaphysis ± bowing of the legs.	

INFANTILE COLIC

Name:
Temperature:Age:
B.P.:Sex:
Pulse:Date:
Resp. Rate:

Definition: a benign condition without any known underlying medical or surgical cause, presenting in between 10 and 30% of infants. It typically begins in the first few weeks of life and resolves spontaneously by 4–5 months of age.



ETIOLOGY

- Unknown
- Age under five years
- Gastrointestinal:** overfeeding or underfeeding, aerophagia, cow's milk intolerance
- Biologic:** ↑ serotonin levels, tobacco exposure, dysfunctional motor regulation related to immaturity
- Psychosocial** (exposure to stress) factors are suspected

△ Infantile colic

C/C:

- Otherwise, healthy infant with appropriate weight gain
- Paroxysmal episodes of loud and high-pitched crying, piercing sound that often occur at the same time each day (usually in the late afternoon or evening)
- Hypertonia (e.g., clenched fists, stretched legs) during episodes
- Difficult to comfort
- Grimacing/frowning
- Excessive gas
- Infant is not easily consoled

On Examination

- Infants are well and growing normally.
- There should be no other findings on examination

Diagnosis: "rule of three"

Characterized by paroxysmal crying:

- Crying for ≥ three hours per day
- Crying for ≥ three days per week, and
- Crying for ≥ three weeks in an infant who is well-fed and otherwise healthy.



- Parental education and reassurance:** The parents must be informed that the infant is not sick, and that excessive crying is a behavioral problem and is not harmful, and that colic will resolve on its own with no long-term adverse effects. Physicians should also offer reassurance that they understand how stressful a colicky infant can be for parents. It usually resolves by sixteen weeks (four months) of age. Continued inconsolable crying in infants can lead to anxiety, frustration, and feelings of inadequacy in parents. These feelings should be acknowledged and properly addressed.

Soothing techniques

- » Rock the baby, hold the baby close or walk with the baby.
- » Stand up, hold the baby close and repeatedly bend your knees.
- » Sing or talk to the baby in a soothing voice.
- » Gently rub or stroke the baby's back, chest or tummy.
- » Offer a pacifier or try to distract the baby with a rattle or toy.

- Physical measures** (rocking, swinging, swaddling, shush & sucking) can be tried, as May dietary changes; response to these measures varies, and often colic resolves only with time.

- Trial of various feeding techniques:** Bottle-fed infants may benefit from a hydrolysed formula, particularly if there is a suspicion that the diagnosis may be cow's milk protein intolerance.

Supportive therapy for symptomatic relief of gas/colic/bloating

Colorest drops or Cholidrop or Pro-Colic drops.

Recommended dosage:

- » Child 1 – 6 months: (0.5 ml) 10 drops – Twice daily
- » Child >6 – 12 months: (1 ml) 20 drops – Twice daily
- » Child 1 – 2 years: (2 ml) 40 drops – Twice daily

Alternative: Beta D-galactosidase drops (Ez-Colic, Sposmad)

CONSTIPATION

Name:

Age:

Sex:

Date:

Temperature:

B.P:

Pulse:

Resp. Rate:



CAUSES OF CONSTIPATION IN VARIOUS AGE GROUPS

Neonatal and infancy

- **Benign:** Insufficient intake of milk and fluids, artificial feeding, delayed introduction of semisolids and solids, prolonged use of laxatives and purgatives
- **Organic:** Hirschsprung disease, congenital hypothyroidism, hypertrophic pyloric stenosis, duodenal atresia, meconium ileus, painful defecation as in anal fissure, intestinal parasitosis, Celiac Disease, cystic fibrosis, anorectal malformations (anteriorly placed anus); spinal cord defects (tethered cord, meningocele)

Childhood:

- **Benign:** Poor dietetic intake, especially low residue diet, dependency on laxatives and purgatives, poor toilet training, unclean toilet, emotional problems
- **Organic:** Intestinal parasitosis, anal fissure, intestinal obstruction (subacute), Celiac Disease, cystic fibrosis

All age groups:

- **Drugs:** Anticholinergics, lead, opiates, phenobarbital, vincristine; abuse of laxatives
- **Dietary:** Low residue diet.

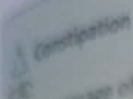
ROME-III CRITERIA FOR FUNCTIONAL CONSTIPATION

Rome III diagnostic criteria for functional constipation in children upto 4 years of age

- Must include one month of at least two of the following:
 - » Two or fewer defecations per week
 - » At least one episode/week of incontinence after the acquisition of toileting skills
 - » History of excessive stool retention
 - » History of painful or hard bowel movements
 - » Presence of a large fecal mass in the rectum
 - » History of large diameter stools which may obstruct the toilet.

Rome III diagnostic criteria for functional constipation in children older than 4 years of age

- Must include two or more of the following:
 - » Straining during at least 25% of defecations
 - » Lumpy or hard stools in at least 25% of defecations
 - » Sensation of incomplete evacuation for at least 25% of defecations
 - » Sensation of anorectal obstruction/blockage for at least 25% of defecations
 - » Manual manoeuvres to facilitate at least 25% of defecations (e.g. digital evacuation, support of the pelvic floor)
 - » Fewer than three defecations per week
- Loose stools are rarely present without the use of laxatives.
- Insufficient criteria for irritable bowel syndrome (IBS).



Constipation

Infrequent passage of infrequent, hard stool.
Overflow faecal incontinence is common and produces small volume, soft stool.
Infrequent, hard stool passed in the absence of any Red Flag symptoms.

Enquire about **RED FLAG SYMPTOMS** specifically.

- » Present from birth
- » Delayed passage of meconium ≥ 48 hours
- » 'Ribbon stools'
- » Neurological symptoms or signs, such as locomotor delay or falling over/abnormal gait in older children
- » Vomiting
- » Abdominal distension

Abdominal Examination: Palpation of the abdomen may reveal an indentable mass, usually in the left lower quadrant (LLQ).

Polyethylene glycol (PEG)-3350

- » Dissolve PEG powder 17 grams in 240 ml water or juice
- » Dose: 0.5 - 0.8 g/kg/day (15 ml/kg/day) up to 17 g/day divided twice daily
- » Adjust dose until 1-2 soft painless stools per day
- » Taper dose over time
- » Efficacy
 - Safe, well tolerated and effective
 - More effective and better tolerated than Lactulose



TREATMENT OF CONSTIPATION

- » All parents and children should receive dietary and lifestyle advice regular, scheduled toileting.
- » Increasing dietary fibre and fluids
- » Increasing exercise.
- » Treatment revolves around the correction of the underlying cause, dietary changes and behavioral training. In general, it needs to be ensured that child takes good deal of high residue diet and fluids and that the parents encourage him to use the toilet regularly.

Polyethylene glycol 3350 (Movicol, MiraLAX)

- » **Dosage:** 0.6 to 1g/kg/day for 3 days
- » **Indicated for 2-11 years of child's with chronic constipation**
- » For children aged 2 to 11 years, the maximum recommended dose needed does not normally exceed 4 sachets a day.
- » **Method of administration:** Each sachet 6.9g should be dissolved in 62.5 ml (quarter of a glass) of water or juice. The correct number of sachets may be reconstituted in advance and kept covered and refrigerated for up to 24 hours. For example, for use in faecal impaction, 12 sachets can be made up into 750 ml of water.

Syp. Lactulose (Duphalac, Lilac)

- » **Dosage:** 1-3ml/kg/day (10mg/15 ml) divided daily to twice daily
- » **Babies aged 1-11 months:** The usual dose is 2.5ml twice a day
- » **Children aged 1-4 years:** The usual dose is 2.5ml-10ml twice a day
- » **Children aged 5-17 years:** The usual dose is 5ml-20ml twice a day

Syp. Prunus domestica (Prune juice) concentrate 1.3g (Prulax)

- » **Children under 5 years:** 1 teaspoonful (5ml) once daily
- » **Children's 5 - 10 years:** 2 teaspoonful (10ml) once OR twice a day.

Syp. Wheat dextrin (Fibo, Fibocon)

- » **Children's upto 5-11 years:** 1 teaspoonful once OR twice a day.
- » **Children's 12 years and above:** 2 teaspoonful once OR twice a day.

For Infant: Glycerin suppository

- » **Preferred agent in age under 1 year (Infant)**
- » **Dosage:** 1/2 to 1 infant suppository (adult suppository for age over 6 years)

Enema

- » **Dosage:** 6 ml/kg (up to 135 ml)
- » May repeat every 12-24 hours for 1-3 doses
- » First dose often given 1 hour before bedtime

If abdominal pain add on

1. Syp. Hyoscine butyl bromide 5mg/5ml (Spasler-P)

Dosage:

- » **Infant:** 1 Teaspoonful (5ml) x 3 times daily
- » **6 years:** 1-2 Teaspoonful (5-10ml) 3 times daily
- » **Over 6 years:** 2 Teaspoonful (10 ml) 3 times daily

DEHYDRATION

Definition: Volume depletion is a deficit in water and solutes from the extracellular portion of total body fluid, leading to a reduction in blood volume. This is different from dehydration, which more specifically indicates a total body water deficit (not enough water in the whole body). In children, the most common cause of dehydration is gastroenteritis, which can lead to severe volume depletion.

Etiologic classification

- **Gastrointestinal (GI) losses:** inadequate intake, diarrhea, vomiting, decreased bowel reabsorption, protein-losing enteropathies, Gastrointestinal (GI) bleeding.
- **Vascular losses:** severe hemorrhage from any area of the body.
- **Renal losses:** impaired water or solute reabsorption due to diabetes insipidus, DM, renal tubular defects, & diuretic use.
- **Increased insensible losses:** loss of skin integrity (in burns), fever, hyperthermia, tachypnea, and physiologic states of high metabolic demand.
- **Extracellular space fluid sequestration:** redistribution of intravascular fluid into the extracellular space, observed in conditions like anaphylaxis, sepsis, small-bowel obstruction, CHF, hepatic failure, and hypoalbuminemia.

ASSESSMENT OF DEHYDRATION

FEATURES	MILD DEHYDRATION	MODERATE DEHYDRATION	
		SEVERE DEHYDRATION	
Mental status	Normal/awake	Restless, Irritable	Lethargic/Unconscious
Eyes	Normal	Sunken	Very Sunken & dry
Capillary refill	Normal	< 3 Seconds	>3 Seconds
Mouth & Tongue	Moist, Wet	Dry	Very dry
Thirst	Drinks normally, not thirsty	Thirsty, drink eagerly	Drinks poorly/not able to drink
Skin pinch	Goes back quickly	Goes back slowly	Goes back very slowly
Pulse	Normal	Faster than normal	Very fast, weak, or you cannot feel it
Breathing	Normal	Rapid	Weak and thready
Urine output	Normal	Deep colour	Scanty
Decisions	The patient has no signs of dehydration	If the patient has two or more signs, including at least one sign, moderate dehydration	If the patient has two or more signs, including at least one sign, severe dehydration
Treatment	Treat as PLAN A	Treat as PLAN B	Treat as PLAN C

TREATMENT OF DEHYDRATION ACCORDING TO WHO & IMNCI GUIDELINES

PLAN-A	• Educated family to use increased amounts of home-based available fluids. Foods high in sugar and carbonated beverages should be avoided. • WHO-recommended – Oral rehydration solutions (ORS) suitable for use. Administer ORS in frequent small volumes, gradually increasing as tolerated. Aim for 50 to 100 mL/kg of ORS over 2 to 4 hours. • Breast fed Infants: Provide breast milk on demand, this may be more frequently than usual. • Older Children: Avoid dairy and fruit juices because they may exacerbate the loose stools. • ORS is administered after every stool. » < 6 months: 50mL (1/4th glass) » 7 months to 2 years: 50 – 100ml (1/4 to 1/2 glass) » 2 to 5 years: 100-200 ml (1/2 to 1 glass) » Later: As much fluid as the child accept. • Asking the parents/caretaker for follow-up after 2 days (even earlier) • Breast feeding should be continued in addition to ORS. • ORS sachets or ORS prepared solution (Pedialyte or Pedicare solution) is advice for use at home.



- Rehydration therapy**
- Correction of existing water and electrolyte deficit
 - 75 ml/kg ORS in first 4 hours**
- Maintenance therapy**
- Replacement of ongoing losses due to continue diarrhea.
 - Start when signs of dehydrations disappear usually in first 4 hours.
 - 10–20 ml/kg ORS for each liquid stool**
- Maintain intravenous (IV) access.
 - Start IV fluid immediately.
 - Recommended IV fluid: Isotonic fluid – Ringer's lactate (Hartmann's solution) or 0.9% N/S. Dextrose solution is not effective.
 - 100ml/kg of fluid is to be given as shown below:
- | Age | First, give 30ml/kg in: | Then, give 70ml/kg in: |
|------------------------|-------------------------|------------------------|
| < 12 months old | 1 hour | 5 hours |
| ≥ 12 months to 5 years | 30 minutes | 2, 1/2 hours |
- Repeat once if the radial pulses are still very weak or not detectable.
 - Reassess the child every 1–2 hours. If hydration status is not improving, give the intravenous drip more rapidly.
 - Also give ORS (about 5 ml/kg/hour) as soon as the child can drink; usually after 3–4 hours (Infants) or 1–2 hours (children).
 - Reassess an infant after 6 hours and a child after 3 hours.
 - Classify dehydration then choose the appropriate plan (A, B, or C) to continue the treatment.

ACUTE DIARRHEA

TREATMENT OF MILD TO MODERATE DIARRHEA

- ASSESSMENT OF DEHYDRATION & TREATMENT OF DEHYDRATION ACCORDING TO WHO & IMNCI GUIDELINES
- Oral rehydration solution (ORS): Mild Dehydration: 50 ml/kg over 4 hours. Moderate Dehydration: 100 ml/kg over 4 hours. Maintenance: Continue ORS after initial rehydration as needed.
- Syp. Zinc sulphate 20mg/5ml (Zincat OD), **Dosage:** WHO dosage of Zinc 10mg per day in infants and those younger than 6 months and 20mg per day for children older than 6 months for 10–14 days
- Racecadotril 30mg sachets (Recada, Hidrasec, Racedo) at dose 1.5 mg/kg orally, three times daily for 5–7 days
- Consider probiotics for maintenance of normal flora:
 - Enterogermina (Bacillus Clausii) oral solution
 - For infants: 1–2 mini bottles per day to be given at regular intervals.
 - For children: 1–2 mini bottles or 1–2 capsules a day to be administered at regular intervals.
 - How to take Oral Enterogermina: Unscrew and remove the top of the cap. Shake it before use. Take the medicine as it is or dilute it with lukewarm water or any other drink such as milk or orangeade.

TREATMENT OF SEVERE DIARRHEA (SEVERE DEHYDRATION)

DOCTOR ON DUTY TREATMENT GUIDE 2024-25 EDITION

- Stabilize patients using ABCD&E approach.
- Establish large-bore intravenous (IV) access.
- Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂ (Check SpO₂ & Give high flow O₂ as appropriate)
- Send Labs: CBC, urea, creatinine, electrolytes, blood glucose, stool analysis and stool culture.
- IV fluid therapy: Ringer Lactate OR 0.9% Normal saline x IV
 - Children <1 year of age: 30mL/kg within first hour followed by 70 mL/kg over next 5 hours.
 - Children >1 year of age: 30mL/kg within half hour followed by 70mL/kg over next two and half hours.
- Correct electrolytes abnormalities
- For patient with vomiting – consider one of the following antiemetic:
 - Inj. Metoclopramide 10mg/2ml (Metaclon, Maxolon) at dose 0.1mg/kg/dose x IV x TDS
 - Inj. Dimenhydrinate 50mg/ml (Gravinate) at dose 0.5-1mg/kg/dose x IV x TDS
 - Inj. Ondansetron 8mg/4ml (Onset, Onseron) x at dose 0.15mg/kg/dose, diluted in 25 to 30 ml of 0.9% NS OR 0.5%W, given by IV infusion over 15 minutes.

BACILLARY DYSENTERY (SHIGELLOSIS)



Risk factors

- » Ingestion of contaminated food or water or direct fecal oral contact.
- » Age < 5 years
- » Malnutrititions
- » Poor hygiene & cramped conditions
- » Travel to endemic areas

Clinical features

SYMPTOMS

- » Duration: 2–7 days
- » Urgency to defecate (tenesmus)
- » Abdominal cramping/pain
- » Profuse inflammatory diarrhea
- » Bloody and mucoid stools
- » Passage of formed feces that temporarily relieves the pain.
- » Features of HUS
- » Febrile seizures, ASOC.

PHYSICAL EXAM

- » Fever
- » Increase bowel sounds.
- » Abdominal tenderness
- » Signs of dehydration

Diagnostic workup

- » CBC: WBCs normal or ↑, ↑ Hct due to volume depletion, leukocytosis.
- » Stool microscopy: leukocytes, RBCs
- » Stool culture and sensitivity: **+ve**
- » BUN and creatinine: suggest AKI.
- » Serum electrolytes if dehydrated.

If there is no improvement 48 hours after starting second-line treatment, treat for amoebiasis: Metronidazole.

- » **Per orally:** Syp. Metronidazole 200mg/5ml OR Tab. Metronidazole 200mg (Flagyl, Klint, Metrozine) at dose 7.5 mg/kg/dose three times a day
- » **Intravenously:** Inj. Metronidazole 500mg/100ml (Flagyl, Klint) at dose 7.5 mg/kg/dose x IV x TDS



TREATMENT OF MILD-MODERATE BACILLARY DYSENTERY

1. **Oral rehydration solution (ORS):** The WHO recommends low-osmolarity ORS formula for diarrhea in all age group patients.
 - » Osmolar ORS (banana or Orange flavoured)
 - » Peditral Low OSM ORS (Lemon/limed or Orange flavoured)
 - » Hilyte-R (Rice based – ORS)
2. **Recommended antibiotics therapy shortens duration of dysentery.**
 - » Syp. Ciprofloxacin 125mg/5ml OR 250mg/5ml (Cipesta, Mytil, Novidate) at dose 15 mg/kg orally twice daily for 3 days. 1–0–1 (BD) for 3 days, (max. 500mg/dose).
 - » OR Syp. Azithromycin 200mg/5ml (Azitma, Zetro, Azomax) at dose 12 mg/kg orally as a single dose on day 1, followed by 6 mg/kg (max. 250 mg/day) once a day for 4 days. 0–0–1 (OD) for 5 days.
 - » OR Syp. Cefixime 100mg/5ml OR 200mg/5ml (Cefim, Cefspan) at dose 8 mg/kg once daily (max. 400 mg daily)
 - » OR Syp. Trimethoprim 80mg/Sulfamethoxazole 400mg (Septran DS) at dose in children ≥2 months of age: 8–10 mg/kg/day orally given in 2 divided doses (BD) for 3–5 days, (max. 160mg/dose)
3. **With fever/pain:** (Calpol 6 Plus, Panadol forte = 250mg/5ml)
 - » Syp. Paracetamol (Calpol = 120mg/5ml, Panadol = 160mg/5 ml)
 - » **Dosage:** 10–15mg/kg/dose x TDS/QID. Maximum 75 mg/kg/day
4. **Supportive therapy:**
 - » **Nutrition:** nutritional supplement with frequent meals
 - » During inpatient: +2500 kcal daily
 - » During outpatient: +1000 kcal daily
 - » **Rehydration:** Advice ORS as per WHO protocols (see Dehydration).
 - » **Zinc supplements** <5 years child. *MSF medical guidelines



TREATMENT OF SEVERE BACILLARY DYSENTERY

1. Consider Hospitalization/early admission.
2. Establish large-bore intravenous (IV) access.
3. Vitals monitoring: Check BP, PR, RR, Temperature, SpO2
4. Obtained labs: CBC, BUN, Creatinine, electrolytes, stool microscopy and stools culture and sensitivity.
5. For severe dehydration or vomiting: Initially isotonic IV fluid as WHO protocol (see dehydration). Once the patient is stable, switch to ORS.
6. **Recommended antibiotics therapy shortens duration of dysentery.**
 - » Inj. Ceftriaxone 2g (Oxidil, Rocephin) x at dose 50–100 mg/kg (Max. 2g/day), diluted in 50–100ml 0.9% NS x IV OD for 5 days.
 - » OR Inj. Ciprofloxacin 400mg/100ml (Novidate DS, Cipesta DS) at dose 15mg/kg orally twice daily for 3 days, (Max. 500 mg/dose).
7. **With fever:** Inj. Paracetamol 1g/100ml (Provas, Paracet) at dose 10–15mg/kg/dose x TDS/QID. Maximum 75 mg/kg/day

LACTOSE INTOLERANCE

DIARRHEA IN CHILDREN'S DUE TO LACTOSE/FORMULA MILK

Lactose intolerance is the reduced ability to digest milk sugars, due to insufficient amounts of the gut enzyme called lactase. Breastfed babies can be lactose intolerant, because lactase is found in breast milk as well as baby formula. Diarrhoea can be a symptom of lactose intolerance in babies.

- » Watery diarrhoea that follows gastroenteritis.
- » Abdominal discomfort and increase flatus.
- » Check the child is growing normally and is hydrated.
- » Abdominal bloating or distension

Treatment for Formula Fed Infants

- » Avoid cow's milk-based formula (i.e. Enfamil Lipil, Similac Advance, Nestle Good Start) until normal stools resume.
- » Soy based (i.e. Prosobee, Isomil) or Lactose free formulas are OK.
- » Offer oral rehydration solutions (Pedialyte)

Rx

- » Switch to lactose-free diet/formula milk
- » Good hygiene, diet and supplementation (Zinc, Calcium, Vitamin-D)
- » If Dehydration: Give ORS to prevent dehydration.

1. Syp. Metronidazole 200mg/5ml (Flagyl, Metrozine)

Dosage: 7.5 mg/kg/dose three times a day (TDS)

OR Syp. Qplex-Z (Gile Armani, Carbohydrate Complex and Zinc)

Dosage: 1 teaspoon 2 to 3 times a day, for older 2 teaspoon.

2. Entrogermina (Bacillus Clausii) oral solution

- » For infants: 1-2 mini bottles per day to be given regularly.
- » For children: 1-2 mini bottles or 1-2 capsules a day to be given.

» How to take Entrogermina oral suspension

- » Unscrew and remove the top of the cap.
- » Shake it before use.
- » Take the medicine as it is or dilute it with lukewarm water or any other drink such as milk or orangeade.

INSTRUCTION

- » Advice yoghurt as it is a natural probiotic, along with banana.
- » Take care of bottle hygiene, use boiled/sterilised bottles each time along with boiled water.
- » Continue use of Zinc for 14 days + Entrogermina for 3-5 days
- » Lactose free milk brands: NL-33, NAN-1, Nutrafil LF, NAN-AL-110, Similac Isomil, Aptamil

HYPOCALCAEMIA

Definition: Total serum calcium below 2 mmol/L=8mg/dl in term newborns and older children or ionized calcium below 1 mmol/L. In Preterm: Total below 1.75 mmol/L

△ Hypocalcemia C/C:

- » Asymptomatic
- » Symptomatic (usually level below 7mg/dl)
 - » Convulsions
 - » Tetany
 - » Hyper Or Hypotonia
 - » Irritability
 - » ICP
 - » Laryngospasm
- » Cardiac:
 - » Bradycardia
 - » Heart failure
 - » Oedema
- » Signs of aetiology

Rx

SYMPTOMATIC

- » Inj. Calcium gluconate 10%/10ml at dose 2ml/kg x IV, dilute 1:4 with 5% Dextrose or water (1:4 = 1ml Calcium + 4ml 5% dextrose), Give IV over 30 minutes
- » ECG monitor (if possible) or clinically for bradycardia or even arrest.
- » Then start infusion of 1mmol/kg /24hours in 5% Dextrose + 1/5 saline OR give the total daily dose divided as 6 hourly infusions
- » Monitor patient and calcium 6 hourly.

IF SYMPTOMS CONTINUE

- » Give another infusion bolus of 1-2 ml/kg OR increase infusion rate to 1.25-1.5 mmol/kg/day

ASYMPTOMATIC

- » After infusion or from the start
- » Oral calcium 1mmol/kg /day
- » 1mmol calcium = 40mg of elemental calcium, Give 6 hourly
- » Check the concentration of preparations in your hospital (Osteocare 5 ml=150 mg)

STATUS EPILEPTICUS



Status epilepticus (SE): It is a life-threatening neurologic condition defined as 5 or more minutes of either continuous seizure activity or repetitive seizures without regaining consciousness. The diagnosis is established after 5 minutes in generalized tonic-clonic seizures and 10 minutes in focal impaired awareness seizures, although long-term neurologic consequences are not likely to occur unless status epilepticus persists for 30 minutes for generalized tonic-clonic seizures or 60 minutes for focal impaired awareness seizures.

Rx

A. Airway:

- » Ensure patient is maintaining own airway. Assess and secure stable airway
- » Suction of the airway to clear secretion - reduced aspiration
- » Intubate (ETT) the patient if status epilepticus or trauma

B. Breathing: Check SpO₂ & Give high flow O₂ as appropriate → SpO₂ should be monitored continuously.

C. Circulation:

- » Establish large-bore intravenous (IV) access (to avoid venous irritation and tissue damage due to phenytoin)
- » Send blood test: CBC, urea, creatinine, electrolytes, LFTs, Blood glucose, calcium, magnesium, phosphorus, ABGs and serum anticonvulsant medication levels (in case of convulsive status epilepticus)
- » Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂
- » Patient with hypoglycemia (glucose <60 mg/dL): Dextrose 25%/25ml ampule or Dextrose 10% in water
 - ↳ Children <2 years of age: Dextrose 12.5%/12.5ml (Half ampule) x 4 mL/kg IV bolus
 - ↳ Children ≥2 years of age: Dextrose 25%/25ml x 2 mL/kg IV bolus
- Alternative option: Inj. Dextrose 10% at rate 4 mL/kg in children <2 years or at rate 2 mL/kg in children ≥2 years IV as bolus, followed by maintenance infusion 6 – 8 mL/kg/minute.

PATIENT WITH ACTIVE SEIZURES/STATUS EPILEPTICUS

➤ First line – Benzodiazepine

- ↳ Inj. Diazepam 10mg/2ml (Valium) x diluted in 8ml 0.9% NS x at dose 0.15mg/kg x IV over 5 minutes as a single dose, may repeat once if necessary (maximum 10mg/dose) OR at dose 0.2 mg/kg (maximum 20 mg/dose) per rectally as a single dose via soft plastic tube attach with 10ml syringe.
- OR Inj. Midazolam 5mg/5ml (Dormicum) at dose 5mg in children's with 13-40kg bodyweight and at dose 10mg in children's with >40kg body weight x IM as a single dose.

➤ Second line – Anti-convulsants (antiepileptics), If seizures continue

- ↳ Inj. Phenytoin 250mg/5ml (Epigran) at dose 15-20mg/kg (maximum 1500mg/dose) in 50 – 100ml 0.9% NS x IV over 15 minutes, may repeat once if necessary.
- OR Inj. Sodium valproate 500mg/5ml at dose 20-40mg/kg (maximum 3000mg/dose) x IV over 15min
- OR Inj. Levetiracetam 500mg/5ml (Epilapsa, Lerace) at dose 30 – 60mg/kg ((maximum 4500mg/dose) x diluted in 20 – 30 ml 0.9% NS x IV over 10-15 min
- ↳ If seizures continue: Inj. Phenobarbital 200mg/2ml (Phenobarb) x at dosage of 15mg/kg x (max 1-1.5 g) x diluted to 20-30mL of 0.9% NS, D5%W or Ringer lactate x IV over 20 minutes

➤ If fail – Third line: Transfer to PICU: Consider General Anesthesia (Midazolam + Propofol, Thiopental)

- ↳ Consult specialist for guidance on anesthetic dose
- ↳ General anesthesia with ventilatory assistance may be required: Inj. midazolam 5mg/5ml (Dormicum) may provide control of refractory status epilepticus; the suggested loading dose is 0.2 mg/kg, followed by 0.05-0.2 mg/kg/hour. Inj. Propofol at dose 1-2 mg/kg/dose as IV BOLUS, followed by infusion at 2-15mg/kg/hr depending on response. Inj. Pentobarbital: may be considered as third line (at dose 5-15 mg/kg x IV, followed by 0.5-4 mg/kg/hr).

D. Disability & Exposure

- » Monitor pupillary reflexes and record GCS level
- » Identify and treat underlying cause, correct electrolytes abnormality
- » Radiology: CT scan/MRI brain (may show hemorrhage, ischemic strokes, edema & tumor, hydrocephalus) & EEG
- » After status epilepticus is controlled, an oral medication program for the long-term management of seizures is started, and investigations into the cause of the disorder are pursued.

FEBRILE SEIZURES

Name: _____ Age: _____ Sex: _____ Date: _____
 Temperature: _____ B.P.: _____ Pulse: _____ Resp. Rate: _____

Definition: Febrile seizures are seizures that are associated with fever; (mainly temperatures exceeding 100.4°F (38°C) in the absence of CNS infection, metabolic abnormalities, or a history of afebrile seizures)

Classification of Febrile seizures

- » **Simple febrile seizures:** Simple febrile seizures are generalized, last less than 15min, and do not recur in a 24-hr period. The most common seizure type is generalized clonic, but atonic and tonic spells are also seen.
- » **Complex febrile seizures:** Complex febrile seizures (focal onset, prolonged, or recurrent within 24 hours) are less prevalent, making up approximately 20 percent of febrile seizures in most series.
- » **Febrile status epilepticus:** Some patients present in febrile status epilepticus (FSE), i.e., continuous seizures or intermittent seizures without neurologic recovery, lasting for a period of 30 min or longer.

INTERNATIONAL LEAGUE AGAINST EPILEPSY (ILAE) CLASSIFICATION OF FEBRILE SEIZURES

Features	Simple febrile seizure (=75%)	Complex febrile seizure* (=25%)
Clinical presentation	» Generalized, usually tonic-clonic seizures (clonic seizures are also possible) » Symmetrical » No other apparent neurologic disorders	» Focal onset » Pronounced on one side of the body » Transient hemiparesis and speech impairment
Duration and frequency	» < 15 minute » Maximum of one seizure within 24 hour	» > 15 minute » > 1 seizure within 24 hour
Age	» 6 months to 5 years	» More commonly outside the typical range of 6 months to 5 years
Postictal phase	» Typically a quick return to normal » Confusion and drowsiness may be present for a short period of time » Prolonged drowsiness or deviated eyes may be a sign of other etiology (e.g., meningitis) or of ongoing seizure activity (see status epilepticus)	

*Febrile seizures are considered complex if at least one of the criteria are met!

DIAGNOSTICS APPROACH TO FEBRILE SEIZURES

- » **Approach to**
 - » Simple febrile seizures do not require specific diagnostic workup
 - » Diagnostic examination focuses on identifying the cause of fever
 - » Complex febrile seizures always require specific investigative tests
- » **Determine the cause of fever**
 - » History and physical examination
 - » **Obtain blood tests:** CBC with differential blood, CRP, electrolytes, blood glucose
 - » **Urine test:** Urinalysis, urine cultures, urine toxicology screen (In suspected cases of intoxication)
 - » **Consider radiological investigation to locate the source of infection:** ultrasound, X-ray
- » **Additional diagnostic steps:** for complex febrile seizures and/or abnormal neurological examination.
 - » **Lumbar puncture:** To exclude meningitis and/or (herpes) encephalitis
 - » **Radiological investigation:** CT scan brain or MRI scan, Electroencephalogram (EEG)

Generally accepted criteria for febrile seizures	Suspicion of meningitis
» A seizure associated with an elevated temperature >100.4°F (38°C) » A child older than 5 months (some says 3 months) to 5 years of age, most commonly 12 to 24 months) » Absence of CNS infection or inflammation. » Absence of acute systemic metabolic abnormality that may produce seizures » No history of previous afebrile seizures	<u>Clinical presentation of meningitis</u> » In infants: Fever and seizures, refusal of feeding, bulging anterior fontanelle, irritability, impairment of level of consciousness and petechiae (meningococcaemia). » In older children: Neck stiffness, Brudzinski's sign, Kernig's sign, fever with or without seizures, impairment of level of consciousness.



TREATMENT OF FEBRILE SEIZURES

- ☐ Stabilize patient using ABCD&E approach
- ☐ Establish large-bore intravenous (IV) access
- ☐ Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂ (Give high flow O₂ as appropriate, if SpO₂ <94%)
- ☐ Send Labs: CBC, urea, creatinine, electrolytes, LFTs, CRP, Blood glucose, calcium and blood culture
- ☐ Child with hypoglycemia (glucose <60 mg/dL): Inj. Dextrose 10% at rate 4 mL/kg in children <2 years or at rate 2 mL/kg in children ≥ 2 years IV as bolus, followed by maintenance infusion 6-8 mL/kg/minute.
- ☐ First simple febrile seizure → Simple febrile seizure generalized, lasts <15 minutes, not repeated in a 24-hour period. Initiate **ANTIPYRETIC THERAPY** with Ibuprofen or Paracetamol.
 - » Oral Ibuprofen in children 6 months to 12 years of age: Syp. Ibuprofen 100mg/5ml (Brufen) OR Syp. Ibuprofen 200mg/5ml (Brufen DS) at dose 5-10 mg/kg orally every 6-8 hours (max dose 40mg/kg/day)
 - » OR Oral Paracetamol: Syp. Paracetamol 120mg/5ml (Calpol, Febrol) OR Syp. Paracetamol 250mg/5ml (Calpol 6 plus, Febrol) at dose 10-15mg/kg orally every 4-6 hours when required. (maxi dose 75mg/kg/day)
 - » OR IV Paracetamol: Inj. Paracetamol 1g/100ml (Provas, Bofalgan) at dose 10-15 mg/kg/dose IV every 4-6 hours when required. (Maximum dose 75 mg/kg/day), Using 10ml syringe or IV chamber.
- ☐ First complex seizure: Antipyretic therapy PLUS Anti-convulsants
 - » Antipyretic therapy: with Oral Ibuprofen or oral/IV Paracetamol (see above simple febrile seizures)
 - » PLUS, Anti-convulsants
 - ☐ Benzodiazepines: Inj. Diazepam 10mg/2ml (Valium) x IV x diluted in 8ml NS OR D5%W (=1mg/1ml) at 0.2mg to 0.3mg/kg/dose x IV, as a single dose, may repeat after 5-10 min if required. Max 10mg/dose OR Inj. Lorazepam 2mg/ml at dose 0.05 mg to 0.1mg/kg x IV, as a single dose, may repeat every 10-15 minutes if required, maximum 4 mg/dose OR Inj. Midazolam 5mg/5ml (Dormicum) at dose 0.1-0.4 mg/kg/dose x IM (Max 10mg/dose)
 - ☐ After the TWO DOSES OF BENZODIAZEPINES if seizures are not controlled: Consider below one
 - Inj. Phenobarbital 200mg/2ml (Phenobarb) x 10-20mg/kg x (1g - 1.5g) x diluted in 20-30ml 0.9% NS x IV over 20 minutes (IV infusion at the rate of 1-2 mg/kg/minute)
 - Inj. Phenytoin 250mg/5ml (Epigran) x 15-20mg/kg/dose in 50-100ml 0.9% NS x slow IV over 20 min
 - Inj. Sodium valproate 500mg/5ml at 25/kg/dose (max 3000mg/dose) at rate of 3-6 mg/kg/min
 - Inj. Levetiracetam 500mg/5ml (Epilapsa, Lerace) x in 20-30ml 0.9% NS x IV over 15-20 minutes.
- ☐ IF SUSPECTED SECONDARY BACTERIAL INFECTION:
 - » Inj. Ceftriaxone 1g/vial (Oxidil, Rocephin, Titan) at dose 75-100mg/kg per day x IV x OD/BD
- ☐ Consider admission in Paediatrics ICU.
- ☐ Monitor pupillary reflexes and record GCS level
- ☐ Investigate, identify and treat the patient for any underlying cause: hypoglycemia, hypocalcemia, hypomagnesemia and infection

INTERMITTENT PROPHYLAXIS

- ☐ Febrile illness with prior history of simple seizure or 1 complex seizure
- ☐ Intermittent prophylaxis to reduce risk of recurrence of febrile seizures effective prophylactics
 - » Benzodiazepine: Oral Diazepam 0.3 mg/kg orally every 8 hours for children > 6 months for 1st 3 days of fever. Alternative: midazolam and clobazam
 - » Anti-pyretic: Paracetamol do not decrease the risk of recurrence

CONTINUOUS ANTIEPILEPTIC PROPHYLAXIS

- ☐ With history of 2 or more complex febrile seizures with ineffective diazepam treatment
- ☐ Continuous prophylaxis with antiepileptic drugs is advocated in the event of failure of intermittent therapy, especially in recurrent atypical seizures or family history of epilepsy.
- ☐ Syp. Sodium valproate 250mg/5ml (Epival) at dose 10-20mg/kg/day OR Syp. Phenobarbitone 20mg/5ml (Debritone) OR Tab. Phenobarbitone 30mg at dose of 3-5mg/kg/day are effective for febrile seizure prophylaxis.
- ☐ CARBAMAZEPINE & PHENYTOIN are ineffective.
- ☐ The duration of therapy should be for 1-2 years or until 5 years of age, whichever comes earlier.

LONG TERM TREATMENT OF CHRONIC EPILEPSY/SEIZURES

PHARMACOTHERAPY WITH ANTIEPILEPTIC DRUGS



The following focuses on the chronic treatment of epilepsy/seizures. The treatment of acute seizures, status epilepticus, neonatal seizures and febrile seizures are discussed above. Antiepileptic drugs raise the seizure threshold that is pathologically lowered in individuals with epilepsy, thereby reducing the risk of future seizures.

Criteria for the choice of antiepileptic drugs (AED): Seizure type, Patient age, comorbidities & contraindications

Consider vitamin-D and calcium supplementation with long-term sodium valproate → ↓ Vit-D → osteoporosis

GUIDELINES FOR CHOICE OF ANTIEPILEPTIC DRUG (AED)

Seizure type		First-line drug	Second-line drugs
Partial (Focal) seizures		» Carbamazepine » Levetiracetam » Phenobarbital (In children)	» Lamotrigine » Oxcarbazepine » Sodium valproate » Brivaracetam » Topiramate » Gabapentin
Generalized seizures	Tonic-clonic (GTCS)	» Sodium valproate » Levetiracetam » Phenobarbital (In children)	» Lamotrigine » Topiramate » Phenytoin » Zonisamide » Carbamazepine » Clonazepam
	Typical absence	» Ethosuximide	» Sodium valproate » Lamotrigine » Clonazepam
	Atypical absence	» Sodium valproate » Levetiracetam	» Lamotrigine » Topiramate » Clonazepam » Felbamate
	Myoclonic		
	Atonic		

COMMON GENERALISED EPILEPSY SYNDROMES

Syndrome	Age of onset	Type of seizure	Treatment
Childhood absence epilepsy	4 – 8 years	Frequent brief absences	Ethosuximide valproate, and Levetiracetam
Juvenile absence epilepsy	10 – 15 years	Less frequent absences than childhood absence	Sodium valproate Levetiracetam
Juvenile myoclonic epilepsy	15 – 20 years	GTCS, absences, morning myoclonus	
GTCS on awakening	10 – 25 years	GTCS, sometimes myoclonus	Diazepam, Lorazepam
Febrile seizure	6m – 5 years	simple or complex seizures	Vigabatrin
Infantile spasm (West synd.)	3 – 12 months	Generalize, subtype type of myoclonic seizure	

GUIDELINES FOR INITIATING ANTIEPILEPTIC DRUGS (AEDS) THERAPY

1. Treatment regimen and principle

- Start anti-epileptic drug after second attack of seizure/fits, after the confirmation or diagnosis of epilepsy type.
- Start treatment with monotherapy (single drug) first-line anti-epileptic drug, should be maintained if possible.
- The lowest possible dose should be given with follow-up every 2 – 3 weeks, titrate the drug dose up slowly (start low, go-slow principle). Increase the dose according to response if needed.
- If seizures control with single first line drug with specific dose → continues same dose for 2 years.
- If the first drug fails (seizures continue or side-effects develop), start second 1st line drug, followed, if possible, by gradual withdrawal (taper off) of first drug slowly.
- Around two-third of epilepsy patients become seizure-free with monotherapy (single drug therapy)
- Combination therapy should only be given if treatment with a single drug fails. In this case, drugs from different classes and/or with different pharmacologic modes of action should be tried.
- If this combination fails, check adherence and reconsider diagnosis: (Are events seizures? Occult lesion? Treatment adherence/alcohol/drugs confounding response?)
- Monitoring with routine test should be done at 1, 3 and 6 months: CBC, LFTs, Urea & creatinine, electrolytes

2. Discontinuance of medication

- Treatment withdrawal may be considered if the patient has <2 seizures/year, an inconspicuous provocation EEG, normal psychological findings, and no hereditary predisposition
- Generally, medication is continued until a minimum of 3–5-year period free of seizures has been established with normal EEG results and Medications should be tapered with caution. Patients should be advised of the risks of recurrence, to allow them to decide whether or not they wish to withdraw. If undertaken, withdrawal should be done slowly, reducing the drug dose gradually over weeks or months.

CHARACTERISTICS OF COMMONLY USED ANTIEPILEPTIC DRUGS IN CHILDREN



Generic name	Brand name with available strength	Initial dose	Maximum dose
Sodium valproate	» Epival, Dapakan, Revalp » Tablets: 250mg, 500mg, Syrup: 250mg/5ml	10-15mg/kg/day	60mg/kg/day
Levetiracetam	» Lerace, Lumark, Recetam » Tablets: 250mg, 500mg, Syrup: 100mg/ml	5-10mg/kg	60mg/kg/day
Carbamazepine	» Tegrol, Seizunil, Epicar » Tablets: 200mg, 400mg, Syrup: 100mg/5ml	5-10mg/kg/day	30 mg/kg/day
Oxcarbazepine	» Trioptal, Telax, Oxalepsy » Tablets: 150mg, 300mg, 600mg	5-20mg/kg/day	40mg/kg/day
Lamotrigine	» Lamictol, Lomogin, Lojin » Tablets: 25mg, 50mg, 100mg	5-15mg/kg/d in patients not taking valproate, 1-5 mg/kg/day in patients on valproate	15 mg/kg/day
Topiramate	» Hitop, Topagen, Torate » Tablets: 25mg, 50mg, 100mg	1-3 mg/kg/day	10 mg/kg/day
Felbamate	» Tab. Felbamate 400mg or 600mg	10 mg/kg/day	45mg/kg/day
Brivaracetam	» Brivatam, Brivace » Tablets: 50mg, 100mg	0.5-2.5 mg/kg/day	5mg/kg/day
Phenobarbitone	» Tab. Phenobarbitone 30mg	2-6 mg/kg/day	10 mg/kg/day
Clonazepam	» Revotril, Naze, Magura » Tablets: 0.5mg, 2mg, Drops: 2.5mg/ml	0.01 – 0.03mg/kg/day	0.2mg/kg/day
Vigabatrin	» Tab. Sabril 500mg	40-100 mg/kg/day	150 mg/kg/day
Phenytoin	» Epitoin Epilantin » Tablet: 100mg, Syrup: 125mg/ml	10-20 mg/kg/day	200 – 400mg
Ethosuximide	» Cap. Ethosuximide 250mg	10-20 mg/kg/day	60mg/kg/day
Gabapentin	» Neogab, Gabix » Capsule: 300mg, 400mg	10-20 mg/kg/day	60mg/kg/day
Zonisamide	» Tab. Zonas 100mg, Tab. Zonegran 100mg	1-2 mg/kg/day	10 mg/kg/day

LONG TERM TREATMENT OF EPILEPSY/SEIZURES

- » **Consult neurology:** Treatment should be managed initially by a specialist neurologist trained in epilepsy.
- » **Remove cause or provoking factors:** Stopping of recreational drug use, treatment of underlying disorders.
- » **Lifestyle changes**
 - » **Aerobic Exercise** (for example running, walking, swimming, or cycling)
 - » **Avoiding of precipitating factors:** Sleep deprivation, ingestion of excessive amounts of caffeine or alcohol
 - » **Psychological approach:** Techniques to abort seizures or reduce seizure frequency for example, avoidance, relaxation, biofeedback, aversive therapy. Promotion of emotional wellbeing for example, yoga. Reduction of psychiatric co-morbidity for example, stress, anxiety or depression. Coping strategies for living with epilepsy for example, cognitive behavioral therapy (CBT), counselling, psychotherapy, educational interventions.
 - » **Ketogenic diet (low-carbohydrate, high- fat):** for patients who cannot tolerate antiepileptic drugs (AEDs) or for seizures that are not completely responsive to AEDs: persistent ketosis, which is believed to play a major role in therapeutic effect. Most commonly used and seems to be most beneficial in children.
- » **Stimulation techniques:** vagus nerve stimulation, deep brain stimulation.
- » **Surgery:** Surgical removal of pathological lesions and Disconnection (surgical section of neuronal circuits)

TREATMENT OF PARTIAL (FOCAL) SEIZURES



Consider one of the following as first-line monotherapy

- Syp. Carbamazepine 100mg/5ml (Tegrol, Seizunil) OR Tab. Carbamazepine 200mg (Tegrol, Seizunil) x initially at dose 5-10 mg/kg orally twice daily (BD), increase the dose gradually every 2 weeks, according to response, maximum 30 mg/kg/day
- OR Syp. Levetiracetam 100/ml (Lerace, Lumark, Recetam) OR Tab. Levetiracetam 250mg OR 500mg (Lerace, Lumark, Recetam) x initially at dose 5-10 mg/kg orally twice daily (BD), increase the dose gradually every 2 weeks, according to response, maximum 60 mg/kg/day
- OR Tab. Lamotrigine 25mg OR 50mg (Lamictol, Lomogin) x initially at dose 1-5 mg/kg orally twice daily (BD), increase the dose gradually every 2 weeks, according to response, maximum 15 mg/kg/day

If first-line monotherapies are unsuccessful consider one of the following second-line monotherapies

- Tab. Oxcarbazepine 150mg, 300mg or 600mg (Trioptal, Telax, Oxalepsy) x initially at dose 5-10 mg/kg orally BD, increase the dose gradually every 2 weeks, according to response, maximum 30 mg/kg/day
- OR Syp. Sodium valproate 250mg/5ml (Epival, Dapakan) OR Tab. Sodium valproate 250mg or 500mg (Epival, Dapakan) x initially at dose 10-15 mg/kg/day orally is given in 1-3 divided doses initially, increase by 5-10 mg/kg/day increments at weekly intervals according to response, maximum 60 mg/kg/day
- OR Tab. Brivaracetam 50mg (Brivatam, Brivace, Brivera) x initially at dose 0.5-2.5 mg/kg/day orally is given in 1 to 3 divided doses, increase the dose gradually every 1-2 weeks, according to response, maximum 5 mg/kg/day.
- OR Tab. Phenobarbitone 30mg at dose 2-6 mg/kg/day orally given in 1-2 divided doses initially, increase gradually according to response, maximum 10 mg/kg/day.

TREATMENT OF GENERALIZED TONIC-CLONIC (GTCS)

Consider sodium valproate as first-line monotherapy

- Syp. Sodium valproate 250mg/5ml (Epival, Dapakan) OR Tab. Sodium valproate 250mg or 500mg (Epival, Dapakan) x initially at dose 10-15 mg/kg/day orally is given in 1-3 divided doses initially, increase by 5-10 mg/kg/day increments at weekly intervals according to response, maximum 60 mg/kg/day

If first-line monotherapy is unsuccessful consider one of the following second-line monotherapies

- OR Syp. Levetiracetam 100/ml (Lerace, Lumark, Recetam) OR Tab. Levetiracetam 250mg OR 500mg (Lerace, Lumark, Recetam) x initially at dose 5-10 mg/kg orally twice daily (BD), increase the dose gradually every 2 weeks, according to response, maximum 60 mg/kg/day
- OR Tab. Lamotrigine 25mg OR 50mg (Lamictol, Lomogin) x initially at dose 1-5 mg/kg orally twice daily (BD), increase the dose gradually every 2 weeks, according to response, maximum 15 mg/kg/day
- OR Tab. Topiramate 25mg, 50mg, or 100mg (Topamax, Hitop, Topagen, Torate) x initially at dose 1-3 mg/kg/day orally given in 2 divided doses, increase according to response, maximum 10 mg/kg/day
- OR Tab. Phenobarbitone 30mg at dose 2-6 mg/kg/day orally given in 1-2 divided doses initially, increase gradually according to response, maximum 10 mg/kg/day.

TREATMENT OF CHILDHOOD TYPICAL ABSENCE EPILEPSY

- Tab. Sodium valproate 250mg/5ml (Epival, Dapakan) OR Tab. Sodium valproate 250mg or 500mg (Epival, Dapakan) x initially at dose 10-15 mg/kg/day orally is given in 1-3 divided doses initially, increase by 5-10 mg/kg/day increments at weekly intervals according to response, maximum 60 mg/kg/day
- OR Syp. Levetiracetam 100/ml (Lerace, Lumark, Recetam) OR Tab. Levetiracetam 250mg OR 500mg (Lerace, Lumark, Recetam) x initially at dose 5-10 mg/kg orally twice daily (BD), increase the dose gradually every 2 weeks, according to response, maximum 60 mg/kg/day

TREATMENT OF TYPICAL ABSENCE, MYOCLONIC, OR ATONIC EPILEPSY

- Syp. Sodium valproate 250mg/5ml (Epival, Dapakan) OR Tab. Sodium valproate 250mg or 500mg (Epival, Dapakan) x initially at dose 10-15 mg/kg/day orally is given in 1-3 divided doses initially, increase by 5-10 mg/kg/day increments at weekly intervals according to response, maximum 60 mg/kg/day
- OR Syp. Ethosuximide 250mg/5ml (Zarontin) at dose 10-20 mg/kg/day orally given in 2 divided doses initially, increase gradually according to response, maximum 40 mg/kg/day
- OR Tab. Lamotrigine 25mg OR 50mg (Lamictol, Lomogin) x initially at dose 1-5 mg/kg orally twice daily (BD) see above

BACTERIAL MENINGITIS

ETIOLOGY

- Neonates
 - 1ST most common causes: Group-B haemolytic streptococcus (*Streptococcus agalactiae*)
 - 2ND most common causes: E-coli
 - 3RD most common cause: *Listeria monocytogenes*
- Children's 2 to 3 months of age: *Neisseria meningitidis* (Meningococcus)
- Children 3 months to 5 yrs: meningococcus, pneumococcus, H. Influenza type-B (uncommon since Hib vaccine)
- Children > 5 years of age: *Neisseria meningitidis* (Meningococcus), *Strept. Pneumoniae* (Pneumococcus)

CLINICAL FEATURES

- Neonates: non-specific features – vacant stare, lethargy, apnoea, poor feeding (refusal to suck), temperature instability (hypo or hyperthermia), respiratory distress, high pitched cry, seizures, bulging fontanelle, shock, rash
- Infants: Fever, lethargy, irritability, poor feeding, vomiting, bulging fontanelle, shock, seizures, coma, rash
- Older children (> 18 months): Fever, headache, drowsiness, vomiting, shock, seizures, & altered mental status
- Meningism: Clinical syndrome of signs and symptoms that are suggestive of meningeal irritation.
 - Signs:
 - Kernig's sign: Pain on lower leg extension, with hip flexed.
 - Brudzinski's sign: Involuntary flexion of knees and hips with neck flexion.
 - Symptoms: headache, neck stiffness and photophobia.

DIAGNOSTIC WORKUP

- CBC: Leukocytosis, anemia, thrombocytopenia
- Inflammatory marker: CRP – Elevated
- BUN & Creatinine: to assess renal function
- Serum electrolytes: Deranged ↓ Ca/Mg
- LFTs: to assess liver functions
- Blood glucose/RBS: ↓ or ↑
- Coagulation profile: Evidence of DIC
- Serum procalcitonin: Normal or elevated
- Blood Culture: (2SETS): Obtain before starting antibiotic therapy – Positive.
- Chest X-ray: may show pneumonia.
- CT scan brain: Normal or raised ICP.
- Lumbar puncture for CSF studies

Bacterial Meningitis CSF analysis	
Appearance	Cloudy, purulent fluid
Cell count	WBC > 1000/mm ³ , Pleocytosis Leucocyte. ↑ Granulocytes.
Lactate	↑↑
Protein	↑ >1.5 g/L; (N <0.5 g/L).
Glucose	↓ <45 mg/dL, or <40%

- CSF culture – Positive
- CSF Gram stain – Positive
- CSF PCR – Positive (useful in distinguishing bacterial from viral meningitis).



TREATMENT OF BACTERIAL MENINGITIS

- Stabilize patients using ABCD&E approach.
- Intubate if GCS <8, the patient has intractable seizures, or there are signs of cerebral herniation e.g. ↑ ICP
- Establish large-bore intravenous (IV) access.
- Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂ (Give high flow O₂ as appropriate, if SpO₂ <94%)
- Send Labs: CBC, urea, creatinine, electrolytes, LFTs, CRP, blood glucose, calcium, magnesium & blood culture.
- Child with hypoglycemia (glucose <60 mg/dL): Inj. Dextrose 10% at rate 4 mL/kg in children <2 years or at rate 2 mL/kg in children ≥ 2 years IV as bolus, followed by maintenance infusion 6-8 mL/kg/minute.



- **Isotonic IV fluid:** 0.9% saline or 0.9% saline with 5% Dextrose
- **Empiric IV antibiotics: DO NOT DELAY ANTIBIOTICS** – should be given as soon as possible for suspected bacterial meningitis (preferably after an LP has been performed). Change antibiotics according to CSF culture.
- **Children age < 3 months:**
 - Inj. Ampicillin (Ampin, Zampilox) at dose 300mg/kg/day in divided doses given every 6 hours
 - PLUS, Inj. Cefotaxime 1g/vial OR 2g/vial (Claforan, Clafort, Cefotax) at dose 200mg/kg/day IV given in divided doses every 6 hours.
- **Children age > 3 months:**
 - Inj. Vancomycin 500mg/vial OR 1g/vial (Vinjec, Vancotic) at dose 15mg/kg IV every 6 hours (QID)
 - PLUS, One of the following
 - Inj. Ceftriaxone 1g/vial OR 2g/vial (Oxidil, Titan, Rocephin) at dose 100 mg/kg/day x IV given in 2 divided doses every 12 hours.
 - Inj. Cefotaxime 1g/vial OR 2g/vial (Claforan, Clafort, Cefotax) at dose 200mg/kg/day IV given in divided doses every 6 hours.
- **Patient with active seizures:** Inj. Diazepam 10mg/2ml (Valium) x IV x diluted in 8ml NS OR D5%W (=1mg/1ml) at 0.2mg to 0.3mg/kg/dose x IV, as a single dose, may repeat after 5-10 min if required, max 10mg/dose (See also treatment of "Febrile convulsion" & "Status epilepticus")
- **Adjunctive corticosteroid:** Ideally, adjuvant dexamethasone should be given with or shortly before the first dose of parenteral antibiotics in all previously well and non-immunosuppressed adults and children. However, it may be given within 4 hours of the first dose of antibiotics.
 - Inj. Dexamethasone 4mg/ml (Decadron) at dose 0.6 mg/kg/day (maximum dose 10mg) 6-hourly for 4 days
- **Gastro-protective covers:** Inj. Omeprazole 40mg/vial (Risek, Ruling) at dose 20mg up to 40mg x IV x OD
- **Vasopressors:** Norepinephrine, Dopamine, Dobutamine, should be given to patients with hypotension or poor perfusion who do not respond promptly to fluid resuscitation.
 - If the patient is hypovolemic or in shock, additional IV fluids must be given.
 - IV fluids should be given cautiously to patients with evidence of elevated intracranial pressure, myocardial dysfunction, or acute respiratory distress syndrome.
- Pass nasogastric (NG) tube and foley's catheter with attachment of urine bag to monitor output

Antibiotics for confirmed meningitis after lumbar puncture with duration

- **Meningococcus:** IV Ceftriaxone (Rocephin, Oxidil, Titan) for 7 days.
- **H. influenzae:** IV Ceftriaxone (Rocephin, Oxidil, Titan) for 10 days for 7 – 10 days.
- **S. pneumoniae:** IV Ceftriaxone PLUS Vancomycin (Vinjec) for 10 – 14 days
- **Group-B Streptococcus (GBS):** IV Cefotaxime (Claforan, Clafort, Cefotax) for ≥14 days
- **Listeria monocytogenes:** IV Ampicillin (Ampin, Zampilox) OR IV Amoxicillin (Supramox, Zeemox, Zoxicillin) for 21 days PLUS IV Gentamicin (Genticin) for at least the first 7 days.
- **Gram-negative bacilli:** IV Cefotaxime (unless alternative directed by local antimicrobial resistance patterns or specific sensitivities) for ≥ 21 days

Contraindications to Ceftriaxone:

Premature neonates with corrected gestational age < 41 weeks and other neonates < 1 month old, particularly those with jaundice, hypoalbuminaemia, or acidosis; or receiving concomitant treatment with intravenous calcium.

Recommended doses for antimicrobials used to treat suspected or confirmed bacterial meningitis

Antimicrobial	Dose	Maximum dose
Ceftriaxone	100mg/kg/day in divided doses administered every 12 hours.	4g/day
Cefotaxime	225-300 mg/kg/day in divided doses administered every 6 to 8 hours.	12 g/day
Ampicillin	300mg/kg/day in divided doses administered every 6 hours	12 g/day
Gentamicin	7.5mg/kg/day in three divided doses	
Vancomycin	60mg/kg/day (15mg/kg/dose) in divided doses administered every 6 hours to achieve trough concentrations of 10 mg/L to 15 mg/L	4g/day
Penicillin-G	300,000 to 400,000 units/kg/day in divided doses given every 4-6 hours.	24 million units/day
Meropenem	120mg/kg/day in divided doses administered every 6 to 8 hours	6 g/day



ACUTE RHEUMATIC FEVER & RHEUMATIC HEART DISEASE (RHD)

CLINICAL FEATURES

- ☞ Constitutional symptoms: Fever, Malaise, Fatigue (common)
- ☞ Joints: Migratory Polyarthrititis (common)
- ☞ Heart
 - » Pancarditis (endocarditis, myocarditis, and pericarditis)
 - » Valvular lesions: most commonly on high-pressure valves
 - ☞ Mitral valve (= 65% of cases):
 - Early mitral regurgitation or prolapse
 - Late mitral stenosis: Rheumatic fever is the most frequent cause of mitral stenosis.
 - Mixed mitral stenosis/regurgitation
 - ☞ Aortic valve (= 25% of cases): Aortic regurgitation, Aortic stenosis (late manifestation)
 - ☞ Tricuspid valve (= 10% of cases)
 - ☞ Dilated cardiomyopathy due to severe valvular disease, myocarditis
- ☞ CNS: Sydenham chorea involuntary, irregular, nonrepetitive movements of the limbs, neck, head, and/or face
- ☞ Skin: Subcutaneous nodules and Erythema marginatum
 - ☞ Erythema marginatum: centrifugally expanding pink or light red rash with a well-defined outer border and central clearing. Painless and nonpruritic.
 - Location: The trunk and limbs are affected; the face is spared. May rapidly appear and disappear at different locations.

DIGNOSTIC APPROACH

- ☞ Revised Jones criteria
 - » Diagnostic criteria for patients with laboratory findings of a preceding GAS infection
 - ✓ Initial episode of ARF: two major criteria or one major plus two minor criteria
 - » Recurrent ARF: either the same as for an initial episode of ARF or the presence of three minor criteria

MAJOR CRITERIA	MINOR CRITERIA
☞ Joints (Migratory Arthritis)	☞ Fever
☞ ♥ 'O' looks like the heart (Carditis)	☞ Antecedent strep infection
☞ Nodules (subcutaneous)	☞ Arthralgias
☞ Erythema marginatum	☞ ↑ ESR (Erythrocyte sedimentation rate)
☞ Sydenham chorea	☞ ↑ CRP (C-reactive protein)
Mnemonic = Jones	☞ First-degree heart block

DIAGNOSTIC WORKUP

☞ Routine test » CBC: Typically shows leukocytosis, anemia » Acute phase reactants ☞ Serum CRP: Elevated, typically ≥ 30 mg/L ☞ Serum ESR: Elevated, typically ≥ 60 mm/hour	☞ Confirmation of GAS infection » Tests showing elevated or rising antibodies ☞ ↑ Antistreptolysin 'O' titer (ASO) ☞ ↑ Antistreptococcal DNase-B titer (ADB) » Positive throat culture for GAS » Positive rapid GAS carbohydrate antigen detection test
☞ ECG: MC prolonged PR interval (first-degree AV block)	☞ Echocardiography: MR > AR (acute), MS (chronic)
☞ X-ray: Enlarge Left atrium & ventricle, Pulmonary edema	



Treatment of Acute rheumatic fever & Rheumatic heart disease (RHD)

- ☞ First line antibiotics: Inj. Benzathine penicillin-G 1.2 million units /vial (Benzibiotic), in child <27kg at dose 6 million units, and in child ≥ 27 kg at dose 12 million units, x IM, every 3–4 weeks, continuous prophylaxis until the ages of 21, after the diagnosis made or for a minimum of 10 years, whichever is longer. In penicillin allergy, consider – Erythromycin or cephalexin
- ☞ Symptomatic treatment of arthritis and fever
 - » NSAIDs: Treatment with an NSAID should continue until all symptoms of acute rheumatic fever have resolved.
 - ☞ Tab. Aspirin 300mg (Disprin) at dose 50–60 mg/kg/day in 5–6 divided doses, up to a Maximum of 80–100 mg/kg/day for 3–4 weeks then tapered gradually depending on ESR/CRP level) – Maximum dose: 4–8g/day
 - OR Tab. Naproxen sodium 250mg (Flexin) for children >2 years of age at dose 10–20 mg/kg/day orally x BD, ^{Max 1g/day}
 - OR Tab/syp. Ibuprofen 200mg (Brufen) for children >6 months of age at dose 5–10 mg/kg x every 8 hours (TDS)
- ☞ Corticosteroids as alternative to NSAIDs or severe cases: Tab. Prednisolone 5mg (Deltacortril) at dose 1–2mg/kg once a day orally for 7 days. (Maximum: 80mg/day). **Not routinely recommended.**
- ☞ PPIs if risk of GI bleed: Cap. Omeprazole 20mg – Initially 0.5mg/kg (max. 20mg) x OD, increased to 2mg/kg (max. 40 mg)
- ☞ Carditis is managed by treating the associated heart failure with diuretics – Tab. Lasix 1–2 mg/kg orally as a single dose, then 0.5–1 mg/kg (to a max of 6 mg/kg) orally every 6–24 hours), ACEIs, fluid restriction, sodium restriction, and bed rest.

HYPOTHYROIDISM

CLINICAL FEATURES

- Even when the thyroid gland is completely absent, most newborns with congenital hypothyroidism appear normal. However, because congenital hypothyroidism is associated with intellectual impairment, thyroid testing is included in the newborn screen and treatment must be initiated as early as possible. Jaundice associated with an unconjugated hyperbilirubinemia may be present in newborns with congenital hypothyroidism.
- **General/Skin appearance:** Fatigue, dry, cool skin, brittle hair, diffuse alopecia, brittle nails, puffy facies and generalized non-pitting edema (myxedema)
- **Metabolic:** Cold intolerance, fatigue, decrease sweating, weight gain despite poor appetite, hyponatremia
- **Nervous system:** Depression, sluggish reflexes, paraesthesia, cerebellar ataxia.
- **ENT:** Dysphagia, Hoarseness of voice.
- **Cardiovascular:** Bradycardia, Dyspnea on exertion, Hypertension (diastolic) and Myxedematous heart disease (dilated cardiomyopathy, bradycardia, dyspnea)
- **Gastrointestinal:** Hypo-defecation/Constipation (decrease GI motility)
- **Urogenital system:** Hyperprolactinemia, Gynecomastia
- **Ocular (eye):** Periorbital edema
- **Musculoskeletal:** Myalgia, Hypothyroid myopathy (proximal weakness, increase CK), carpal tunnel syndrome, myxedema (small lump rising on the surface of a muscle when struck with a hammer), short stature, delayed bone age and retarded dental eruption, hypotonia and a slow relaxation component of deep tendon reflexes
- **Goiter** (in Hashimoto thyroiditis) or **atrophic thyroid** (in atrophic thyroiditis)

DIAGNOSTIC WORKUP

- 1) **Thyroid function tests (TFTs):** (Free T3, Free T4 & TSH level)
 - » Send TSH level for all patients: ↑ TSH with classic clinical features is typically diagnostic for primary hypothyroidism (TSH is best initial screening test).
 - » If TSH level is abnormal, send Free T4 (FT4). FT4 ↓ is confirmatory test for primary hypothyroidism if TSH is raised.

Interpretation of TFTs in suspected hypothyroidism

Type	TSH	FT4	FT3
Subclinical hypothyroidism	↑	N	Normal(N)
Primary hypothyroidism	↑	↓	Normal/↓
Secondary hypothyroidism	↑	↓	Normal/↓
Tertiary hypothyroidism	↓	↓	Normal/↓

2) Antibody Testing

- » **Thyroglobulin Antibody (Tg-Ab) and Thyroid Peroxidase Antibody (TPO-Ab):** Detectable in most patients with autoimmune hypothyroidism.
- » **TSH Receptor Antibody (TR-Ab):** +ve in up to 20%

Autoimmune hypothyroidism

↑ TSH, FT4 ↓ & TPO Antibodies +ve

- 3) **Radioactive iodine uptake test:** Measures the proportion of exogenous iodine that is taken up by the thyroid (normally 10-35%). Decreased uptake indicates hypothyroidism.

- 4) **Ultrasound thyroid:** Useful for the assessment of thyroid vascularity, goiters, and thyroid nodules

5) Baseline investigation for associated condition

- » CBC: mild anemia
- » Blood sugar level: ↓ (Hypoglycemia)
- » Serum electrolytes: maybe abnormal (↓ sodium)
- » Fasting lipid profile: ↑ LDL, hyperlipidemia
- » Creatine kinase: ↑ in hypothyroid myopathy

TREATMENT OF HYPOTHYROIDISM

- 1) **General Principles:** Lifelong replacement, Prompt initiation
- 2) **Tab. Levothyroxine 50mcg or 75mcg or 100mcg** (Thyronorm) at dose 75-100 mcg/m²/day) is the drug of choice for acquired hypothyroidism. In neonates with congenital hypothyroidism, the recommended initial dose is 10-15 mcg/kg/day. Serum total T4 or FT4 concentrations are used to monitor the adequacy of initial therapy because the high neonatal TSH may not normalize for weeks. Subsequently, serum T4 and TSH are monitored in combination
- 3) **Standard dosages:**
 - » 0-3 months: 10 mcg to 15 mcg/kg/day
 - » 3-12 months: 6 mcg to 10 mcg/kg/day
 - » 1-3 years: 4 mcg to 6 mcg/kg/day
 - » 3-10 years: 3 mcg to 5 mcg/kg/day
 - » 10-16 years: 2 mcg to 4 mcg/kg/day
 - » >16 years: 1.6 mcg/kg/day



HYPERTHYROIDISM & THYROTOXICOSIS

CLINICAL FEATURES

- **General/Skin appearance:** Weakness, fatigue, warm, moist skin, fine hair, onycholysis, Infiltrative dermopathy, especially in the pretibial area (pretibial myxedema).
- **Metabolic:** Heat intolerance, increase sweating, weight loss despite good appetite.
- **Nervous system:** Hyperactivity, restlessness, anxiety, insomnia, depression, fine tremors, hyper-reflexia (brisk)
- **Cardiovascular:** Tachycardia, palpitations, dyspnea, irregular pulse (due to Atrial Fibrillation/Ectopic beats), chest pain and hypertension (systolic)
- **Gastrointestinal:** Hyper-defecation/diarrhea, Frequent bowel movements (increase gastro-intestinal motility)
- **Urogenital system:** Hyperprolactinemia, gynecomastia
- **Ocular (eye):** Ophthalmopathy in Graves' disease (including periorbital edema, exophthalmos), lid retraction (staring look)/lid lag (increase sympathetic stimulation of levator palpebrae superioris & superior tarsal muscle)
- **Musculoskeletal:** Thyrotoxic myopathy (proximal weakness, normal CK), osteoporosis/Increase fracture rate (T3 directly stimulates bone resorption)
- **Goiter:** Diffuse, smooth, nontender goiter; often audible bruit at the superior poles. Also seen in subacute thyroiditis, toxic adenoma, and toxic Multi nodular goiter

DIAGNOSTIC WORKUP

- **Thyroid function tests:** Initial screening test: TSH level – low/undetectable; a normal TSH level usually rules out hyperthyroidism.
Interpretation of thyroid function test
 - ↓ TSH, ↑ Free T4: Primary hyperthyroidism/Thyrotoxicosis
 - ↓ TSH, Normal Free T4 and total T3: Mild or subclinical hyperthyroidism/thyrotoxicosis
 - ↓ TSH, Normal Free T4, ↑ total T3: T3 hyperthyroidism/thyrotoxicosis
 - Normal or ↑ TSH, ↑ Free T4 and ↑ total T3: Thyrotropic adenoma (TSH-secreting pituitary adenoma)
- **Baseline Investigation**
 - CBC: Leukocytosis and/or mild anemia
 - LFTs: Mildly elevated AST, ALT, ALP and bilirubin
 - Fasting lipid profile: ↓ total cholesterol, LDL, and HDL
 - Blood sugar level: Hyperglycemia
 - Serum Calcium level: Mild hypercalcemia
 - ESR: typically, ↑ (> 100 mm/hour) in subacute thyroiditis
 - TSH Receptor Antibody (TRAb): if Graves' disease is suspected but classic clinical features are absent
 - ECG: Tachycardia, Atrial fibrillation, LBBB and ECG signs of LVH in patients with dilated cardiomyopathy
 - Nuclear medicine thyroid scan and Radioactive iodine uptake measurement: First-line test for most patients with uncertain etiology of thyrotoxicosis after initial evaluation
 - Thyroid ultrasound with Doppler: Palpable abnormality, e.g., goiter or nodules
 - Ultrasound-guided FNAC
 - Chest PA and Lateral x-ray demonstrates thyroid enlargement due to goiter.



TREATMENT OF HYPERTHYROIDISM

1. Strenuous physical activity should be avoided in untreated hyperthyroidism.
2. Tab. Propranolol 10mg (Inderal, Cardinal) x BD OR TDS
 Dosage: 0.5mg to 2mg per kg per day x two or three times daily

3. Tab. Carbimazole 5mg (Neomarcazole)

» Dosage: Dose typically used is 0.2mg – 0.5mg/kg/day (or 1.0mg/kg/day)

» Fixed doses:

» Infants: 1.25mg/day

» 1 – 5 years: 2.5mg to 5.0mg per day

» 5 – 10 years: 5.0mg to 10mg per day

» 10 – 18 years: 10mg – 20mg per day

» With severe clinical or biochemical hyperthyroidism, doses that are 50% – 100% higher than the above can be used.

Treatment guidelines

- » Clinical response in 2 – 3 weeks
- » Adequate control in 1 – 3 months
- » Durations: 5 years

AUTISM SPECTRUM DISORDER (ASD)

- Definition: Autism spectrum disorder (ASD) is a lifelong neurodevelopmental condition characterized by qualitative impairment in social interaction and communication as well as repetitive stereotyped behavior, interests, and activities. These features are present early in development and cause impairment of social and academic functioning.
- Prevalence: 14.7/1000 in the USA, Sex: Male > female (4:1), Age of onset: Symptoms typically manifest before 2-3 yrs of age.

ETIOLOGY

- The etiology of autism spectrum disorder is complex and multifactorial.
- The following factors have been identified:
 - Strong factors: Male sex, positive family history, gestational valproate exposure and genetic variant
 - Genetics: Strong underlying predisposition. Many genes have been found to be associated with autism/ASD
 - Environmental factors (e.g., toxin exposure, prenatal infections), May increase the risk of autism spectrum disorder (ASD). However, no specific causes have been identified.
- Studies have shown that there is no link between the MMR vaccine and autism.

CLINICAL FEATURES

- Core features:
 - Persistent deficits in social communication and social interaction in multiple setting:
 - Lack of Social-emotional reciprocity (lack of awareness or understating of the thoughts or feeling of others)
 - Impairment in developing, maintaining, and understanding relationships
 - Abnormal language development, reduced empathy, difficulties in adjusting behavior to social situations
 - Lack of non-verbal communication behaviors (Poor eye contact and facial expression)
 - Restricted, repetitive patterns of behavior, interests, and activities:
 - Hand flapping, excessive touching/smelling, lining up toys, adverse response to sounds, and echolalia
 - Motor movements that are stereotyped or repetitive (e.g., stereotyped hand movements, flipping objects)
 - Unwavering adherence to routines, inflexibility to change
 - Highly restricted, fixated interests, self-injurious behaviors.
- Additional features: Intellectual impairment, Language impairment, feeding difficulties, **Sensory interest**: visual (looking at lights, from corner of eye at objects, examining objects more closely than expected); tactile (touching or stroking objects or people); olfactory (smelling objects, or familiar or unfamiliar people); gustatory (licking or tasting objects or people) and **sensory difficulties** (negative and sometimes idiosyncratic reaction to certain textures, sounds, and other sensory stimuli)
- These symptoms must be present in the patient's early developmental period in the absence of organic etiology (hearing dysfunction). These symptoms cannot be better explained by other conditions (e.g., intellectual developmental disorder)
- Associated conditions:
 - Epilepsy
 - Other neurodevelopmental and psychiatric disorders: e.g., ADHD, Pica, anxiety disorder
 - Genetic disorders: e.g., tuberous sclerosis, fragile X syndrome, Rett syndrome
 - Associated with a higher head circumference to brain volume ratio

DIAGNOSTIC APPROACH

- Diagnosis is based on careful assessment/Comprehensive evaluation of: Social interaction and communication skills, Language and comprehension skills, Behavior, Cognitive development
- Associated conditions
 - Hearing and vision testing: to rule out comorbidities or other causes of developmental delays and behavioral disorders.
 - Genetic testing: fragile X syndrome, tuberous sclerosis (if any of these conditions is suspected)

TREATMENT OF AUTISM

- Early behavioral and educational management
 - Should be started already in preschool (greatly improves outcomes) – 12 months to 5 years of child.
 - Competence training: Social skills, total communication skills
 - Family support and counseling: Parental education on interaction with the child & acceptance of his/her behavior)
 - Multidisciplinary therapies such as speech-language therapy, occupational therapy, and physical therapy
- Pharmacological treatment:
 - SSRIs for Repetitive stereotyped behavior, Anxiety and mood. SSRIs followed by Antipsychotic if no response UK guidelines
 - Syp. Fluoxetine 20mg/5ml (Depricap, Rize) at dose 5mg at AM x OD increase gradually up to 20mg if no response
 - Syp. Escitalopram 10mg/ml (Citanev, Prolexa) at dose 2.5mg AM x OD increase gradually up to 10mg if no response
 - Antipsychotic drugs for Repetitive stereotyped behavior Aggression, Self-injury and overactivity
 - Syp. Risperidone 1mg/ml (Risp, Persch, Risperdal) at dose 0.5-3mg/day (Monitor for EPS, treated with Procyclidine)
 - Methylphenidate for Attention deficit hyperactivity disorder (ADHD) → hyperactivity and inattention
 - Tab. Methylphenidate 10mg (Phenida, Ritalin, Madalin) at dose 5mg at AM OD up to 20-30mg x BD

CEREBRAL PALSY (CP)



Definition: Cerebral palsy (CP) is an umbrella term referring to a non-progressive damage to the brain originating during the prenatal, neonatal, or early postnatal period (when brain neuronal connections are still evolving) that results in disorders of movement and posture development. Depending on the affected brain area, spastic, ataxic, or dyskinetic CP develops.

Epidemiology: Most common motor disability (80%) in children, affecting approximately 2/1000 births in developed countries.

Etiology: Idiopathic (most cases)

Risk factors:

1. Preterm birth and low birth weight (most important risk factors)
2. TORCH infection, Intracranial hemorrhage
3. Perinatal asphyxia, birth asphyxia
4. Structural abnormality of the brain
5. Neonatal seizures and Kernicterus
6. Postnatal infection (e.g., meningitis, encephalitis)

Differential diagnoses

- » Hypothyroid myopathy
- » Mitochondrial myopathy
- » Progressive muscular dystrophies
- » Myelomeningocele
- » Traumatic peripheral nerve lesions
- » Genetic syndromes

Classification of cerebral palsy

Spastic cerebral palsy: spastic paresis of one or more limbs (75% of cases)

Non-spastic cerebral palsy:

- » **Dyskinetic:** abnormal involuntary movements (choreoathetoid, dystonic)
- » **Ataxic:** intention tremor, lack of balance and coordination

Clinical features

All types:

- » Patients do not reach certain milestones
- » Intellectual disability (50%)
- » Seizure disorder (35-50%)
- » Joint contractures
- » Attention deficit hyperactivity disorder

Spastic type:

- » Muscle tone in one or more limbs: ↑
- » Deep tendon reflex: ↑
- » Persistence of primitive reflexes: +ve Babinski sign
- » Toe walking or equinus deformity
- » Muscle weakness and/or atrophy
- » Scissor gait: due to spastic paraplegia of the hip adductors
- » Hip dislocation and Scoliosis
- » Hearing or vision impairment

Non-spastic type:

- » Abnormal involuntary movements that worsen with stress and disappear with sleep
- » Chorea
- » Athetosis
- » Dystonia and Ataxia
- » Dysarthria and dysphagia

Diagnostic workup

History and physical examination: Diagnosis is mainly based on the clinical presentation. Patients may present with mixed types of cerebral palsy (e.g., combination of spastic and athetoid Cerebral Palsy).

Diagnostic investigation is mainly based on the clinical picture.

- » **Cranial USG (early neonatal period):** Intracerebral hemorrhage and/or hypoxic-ischemic injury, structural abnormalities
- » **MRI (in older infants):** to detect causative lesion → periventricular leukomalacia, congenital malformation, stroke or intracranial hemorrhage, cystic lesions. Every child with an equivocal diagnosis of CP should have an MRI brain.



TREATMENT OF CEREBRAL PALSY (CP)

There is no curative therapy for cerebral palsy. Treatment is dependent on the severity and nature of symptoms. A multi-disciplinary approach is employed in management to improve function and quality of life. Pediatricians can guide families in developing a treatment plan starting with a discussion of the family's and child's goals.

Non-pharmacological management/multidisciplinary approach: Physical therapy (prevent muscle contractures), Occupational therapy (motor skill development), Speech therapy (communication skills & dysphagia), Orthotic devices (e.g., braces, splints, and casts) and Assistive devices (e.g., wheelchairs, walkers), Educational support (for intellectual disability), Nutritional support (for eating, drinking and swallowing difficulties), Social support & psychological support.

Pharmacological management

1. **Antispasmodics (Diazepam, baclofen, Sinamet):** reduces muscle tone and often improves mobility.

- » **Tab. Baclofen 10mg (Baclast, Lioresal)**

- » Children 2-7 years of age: 5mg, orally TDS, increase gradually according to response up to 40mg/day

- » Children ≥8 years of age: 5mg, orally TDS, increase gradually according to response up to 60mg/day

- » **Inj. Botulinum toxin-A** (reduces localised spasticity, cervical dystonia) – Refer specialist for guidance on dose

2. **Epilepsy control with Anticonvulsants:** Levetiracetam, Sodium Valproate (See treatment of seizures)

3. **For rigidity and sialorrhea:** Anticholinergics (Hyoscine hydrobromide, Trihexyphenidyl HCL, Glycopyrronium bromide)

4. **Neuro-protective:** Syp. Piracetam (Neutrophil), Syp. Citicoline (Citolin) x 5 – 10ml x OD/BD (Off-label use)

5. **For prevention of osteoporosis (Calcium & Vit-D supplement):** Syp. Calone-D, OR Syp. Osteocare x 5 – 10ml x OD

6. **Analgesia and pain control:** Paracetamol, NSAIDs (Brufen), steroids

7. **Respiratory problems particularly pneumonia** – consider antibiotics see Pneumonia in children's

BELL'S PALSY (FACIAL NERVE PARESIS/7TH CN PARALYSIS) IN CHILDREN

Definition: Bell palsy (In Urdu "LAQWA = لاگو") is an idiopathic facial paresis of lower motor neuron type that has been attributed to an inflammatory reaction involving the facial nerve near the stylomastoid foramen or in the bony facial canal.

ETIOLOGY

- Idiopathic (most common cause of peripheral facial nerve palsy):** Acute idiopathic peripheral facial palsy
- Secondary causes/Risk factors:**
 - Infection:** Herpes zoster (Ramsay Hunt syndrome), Borreliosis (Lyme disease), HSV reactivation, HIV, Malignant otitis externa, Influenza virus (due to intranasal influenza vaccine) and URTI
 - Trauma** (e.g., temporal bone fracture), **Tumors** (parotid gland tumors, acoustic neuroma)
 - Other risk factors include:** Pregnancy, Diabetes mellitus, Hypertension, Guillain-Barré syndrome (GBS), Sarcoidosis (Heerfordt syndrome), Amyloidosis, dental procedures and Stroke

Clinical features

Central vs. peripheral facial nerve palsy

Motor signs in central and peripheral facial palsy

Clinical feature	Central (signs are contralateral to the lesion)	Peripheral (signs are ipsilateral to the lesion)
Ability to frown or lift eyebrows	Intact	Impaired
Ability to close the eyelids completely	Intact	Impaired
Mouth drooping	Present	Present

Additional signs of peripheral facial palsy

- Sensory disturbances:** Pain: Painful sensation around (Postauricular pain) or behind the ear or otalgia, impairment of taste in the anterior tongue, Hyperacusis
- Dry mouth** (as a result of decreased saliva production)
- Ocular features:** Bell's phenomenon, Lagophthalmos, Decreased lacrimation, Keratoconjunctivitis sicca (dry eye), Corneal ulceration and keratitis (inflammation of the cornea), Ectropion
- Facial synkinesis:** Involuntary movements of the facial muscles (facial spasms while closing the eyes)

Diagnostic workup

- History and physical examination:** Clinical diagnosis of exclusion, based on history and physical examination alone → acute, unilateral facial palsy, with an otherwise normal physical examination.
- Investigations ARE NOT ROUTINELY NEEDED – see neurology section for detail**
 - CBC with differential:** exclude leukaemia should be considered in all patient's presenting with suspected Bell's palsy
 - Serologic tests for Lyme disease** should be done when the history of patient suggests exposure to ticks/tick bite
 - CT or MRI** should be considered if there are any red flags of atypical features.

TREATMENT OF BELL'S PALSY (FACIAL NERVE PALS) IN CHILDREN

Symptomatic therapy

- Provide symptom-based treatment for all patients** (regardless of the cause).
- Initiate eye protection:** artificial tears, eye lubricant drops/ointment, and/or taping or patching of the eye
- Incomplete mouth closure:** Advise the patient on proper lip and mouth care.
- Persistent facial nerve paresis (≥ 3 months):** Consider physical therapy and facial reconstructive options.

Targeted treatment

- Idiopathic facial nerve palsy is self-limited**, approximately 60% recover completely without treatment but early treatment is recommended with corticosteroids to increase the chance of complete recovery.
- Oral corticosteroids:** Consider for all patients (regardless of severity) within 48–72 hours of symptom onset.
- Guidelines:** Historically, adult data has been extrapolated and applied to children. There have been very few studies of sufficient quality that have examined whether steroids are of the same benefit in children with Bell's Palsy.
- Syp. Prednisolone 5mg/5ml OR Tab. Prednisolone 5mg** (Deltacortril, Rapicort) at dose 1mg/kg per day for 7–10 day (maximum dose 50mg/day), prednisolone treatment was subsequently tapered off within the next 3–5 days.
- Consider adding an antiviral to steroid therapy**, if there is evidence of herpetic vesicles in the external ear canal. (Do not use antiviral as monotherapy): **Syp. Acyclovir 200mg/5ml** (Acylex) OR Tab. Acylex 200mg or 400mg x In children >2 years of age at dose 80mg/kg daily divided every 6 hours for 5 days, with a maximal daily dose of 3,200mg/day OR Tab. Valacyclovir 500mg (Valtrex) x In children >2 years of age at dose 20mg/kg three times per day, up to a maximum of 1000mg three times daily for 5–7 days (aafp.org/pubs/afp/issues/2007/1001/p997)
- For secondary facial nerve palsy treatment of underlying cause or refer to sub-specialty**
- Follow up every 1–2 week with pediatrician/specialist &/or advanced test**, if the patient has any of the following:
 - No signs of improvement in 2–3 weeks
 - Persistent (≥ 3 months), progressive, and/or recurrent symptoms



POSTSTREPTOCOCCAL GLOMERULONEPHRITIS (PSGN)

- Definition: Poststreptococcal glomerulonephritis (PSGN) is an acute glomerular inflammation characterized by rapid deterioration of the kidney function due to an inflammatory response (type III HSR) following streptococcal infection. This condition results from specific strains of group 'A' beta-hemolytic streptococci (GAS) called nephrogenic streptococci. The disease affects the glomeruli and the small blood vessels of the kidneys.
- Age of onset: Mostly affects children (between the ages of 3–12 years) and patients > 60 years of age

ETIOLOGY

- Prior infection with group 'A' beta-hemolytic streptococci (GAS)
- Site of infection in children
 - After throat infection (tonsillitis, pharyngitis): PSGN typically arises 1–2 weeks following infection
 - After soft tissue/skin infections (erysipelas, impetigo): PSGN typically arises 4–6 weeks following infection.
 - After osteomyelitis

CLINICAL FEATURES

- Approximately 50% of patients remain asymptomatic.
- Symptoms occur approximately 1–6 weeks following an acute infection.
- Nephritic syndrome
 - Hematuria: cola colored urine
 - Edema (prominent facial edema)
 - Hypertension: can lead to headaches
 - Oliguria defined as a urine output that is less than 1 mL/kg/h in infants, less than 0.5 mL/kg/h in children.
- Influenza-like symptoms: Fever, chills, malaise, anorexia, nausea
- Flank pain: Pain in one side of the body between the upper belly area (abdomen) and the back.

DIAGNOSTIC APPROACH

- Initial workup for glomerular disease:
 - Urinalysis and microscopy of urine sediment: nephritic sediment
 - Hematuria with RBC casts: Red cell in urine ++ve
 - Proteinuria: Protein in urine ++ve
 - Pyuria: Pus cells in urine ++ve
 - Quantification of proteinuria: Typically shows non-nephrotic range proteinuria
 - Urine protein/creatinine ratio: usually < 300 mg/g
 - 24-hour urine collection (less commonly obtained): usually 0.3–3.4 g/24h, indicates nephrotic-range proteinuria
 - BUN & creatinine: ↑ indicates severe or advanced disease. Normal level does not exclude significant renal pathology.
 - Estimated glomerular filtration rate (eGFR): Normal or reduced. The eGFR gives an indication of the severity and stage of chronic kidney disease. More accurate than creatinine alone.
 - Serum electrolyte abnormalities
 - Erythrocyte sedimentation rate (ESR): non-specific, Elevated or normal
 - Complete blood count (CBC): May show normocytic, normochromic anemia
 - Fasting lipid profile: Hyperlipidemia or normal
 - Complement levels: Classically shows decrease C3 complement with normal C4 complement
 - Ultrasound renal: typically normal; may show nonspecific increased echogenicity of the renal cortex
- Confirmatory of GAS infection
 - Antistreptococcal antibody titers (ASO titers) → Indicated in all patients with suspected PSGN
 - Findings: ↑ ASO titers (Normal <200), ↑ anti-DNase B antibodies, ↑ Antihyaluronidase antibodies
 - Isolation of group A beta-hemolytic streptococci → Indicated in suspected active GAS infection
 - Diagnostics: Pharyngitis → rapid strep test, throat culture and Skin lesions → wound cultures



TREATMENT OF POSTSTREPTOCOCCAL GLOMERULONEPHRITIS (PSGN)

Principles of management

- Most patients of PSGN are self-limiting and complications of volume overload are managed with supportive treatment.
- Nephrology consultation to develop a treatment plan.
- Admit patients with any of the following indications of severe disease: Patient indicated for dialysis, Moderate to severe acute kidney injury (AKI) or progressive renal failure. Hypertensive crisis (e.g., neurological symptoms of posterior reversible encephalopathy syndrome)
- Management of associated symptoms (e.g., edema, hypertension) as needed.
- Treatment of current active infection, if present (e.g., positive cultures for GAS) → Antibiotic regimens for acute GAS
- Monitor: B.P., creatinine, electrolytes, urinalysis, urine protein, and complement levels until they return to baseline.



1. Management of edema and volume overload

- Low-sodium diet: < 2 g/day
- Fluid restriction (e.g., < 2 L per day)
- Loop diuretics: Furosemide 40–120 mg/day orally given in 1–2 divided doses, adjust dose according to response, maximum 600 mg/day; 20–40 mg intravenously/intramuscularly as a single dose initially, increase by 20 mg/dose every 2 hours according to response, individually determined dose should be administered once or twice daily

2. Anti-hypertensive: Indicated for hypertension refractory to management of edema and volume overload

- Calcium channel blockers: Nifedipine
- ACE inhibitors (Enalapril, Ramipril, Captopril) OR ARBs (Candesartan, Losartan)
 - Uncertain benefit, given the self-limited nature of PSGN
 - Avoid in patients with rapidly progressive renal dysfunction.
 - Consider in patients with concomitant proteinuria, unless there are contraindications for ACE inhibitors & ARBs
 - Requires close monitoring with creatinine & electrolytes as these drugs can exacerbate AKI & hyperkalemia

Dosages:

Tab. Enalapril 2.5 to 5mg orally OD initially, increase gradually according to response, maximum 40mg/day.

Tab. Ramipril 1.25 to 2.5mg orally OD initially, increase gradually according to response, maximum 20 mg/day

Tab. Candesartan 8–16 mg orally OD initially, increase gradually according to response, maximum 32 mg/day

Tab. Losartan 25–50 mg orally OD initially, increase gradually according to response, maximum 100mg/day given in 1–2 divided doses

SCABIES

Scabies

C/C:

- Incubation period: Approximately 3–6 weeks following infestation.
- Intense pruritus that increases at night
- Burning sensation
- Skin lesions
 - Elongated, erythematous papules
 - Burrows of 2–10 mm in length
 - Scattered vesicles filled with clear or cloudy fluid
 - Excoriations, pustules, & secondary infection
- Predilection sites
 - Wrists (flexor surface)
 - Medial aspect of fingers
 - Interdigital folds (hands and feet)
 - Male genitalia (e.g., scrotum, penis)
 - All other intertriginous areas of the skin (anterior axillary fold, buttocks)
 - Periumbilical area or waist
 - Additionally in children, elderly persons, and immunosuppressed patients: scalp, face, neck, under the nail, palms of hands, & soles of feet



- Treatment of Close Contacts: Treat all household members and close contacts simultaneously, even if asymptomatic, to prevent reinfestation.

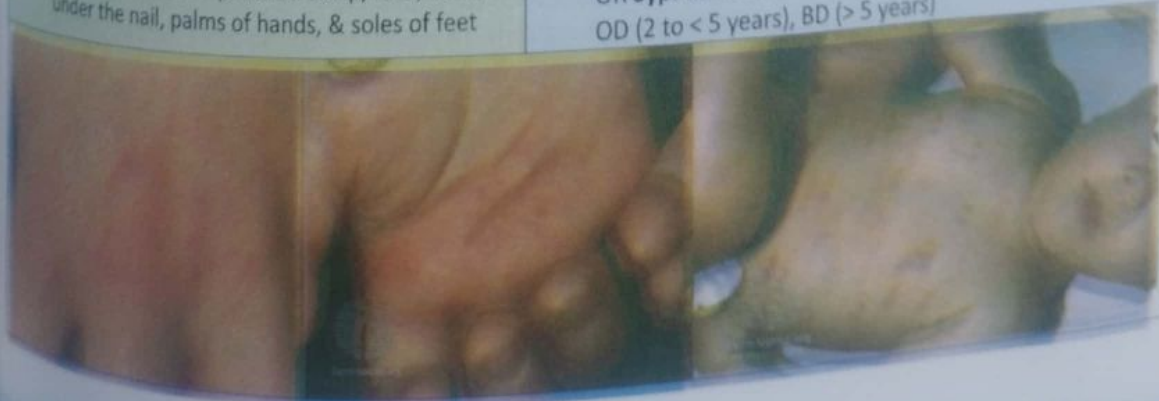
Cleaning and Disinfection

- » Wash all clothing, bedding, and towels used by the infected child in hot water and dry on high heat.
- » Items that cannot be washed should be sealed in a plastic bag for at least 72 hours to kill mites.

1. Permethrin 5% Cream, Lotion (Lotrix, Mitonil)

- » Apply a thin layer to the entire body from the neck down, including under the nails.
- » In infants & young children, also apply to the scalp & face, avoiding the area around the eyes & mouth.
- » Leave on for 8–14 hours, then wash off.
- » Repeat the treatment after 7–10 days if necessary.

2. Antihistamines: Syp. Loratidine 5mg/5ml (Softin, Loril) OR Syp. Levocetirizine 5mg/5ml (Belair, Xyzal) OD (2 to < 5 years), BD (> 5 years)



IMPETIGO

- Definition: Impetigo is a highly contagious superficial bacterial infection typically caused by *Staphylococcus aureus* (most common) and less commonly by *Streptococcus pyogenes* with lesions that evolve from papules to Vesicles to pustules, which eventually break down to form characteristic "honey-colored" crusts. It has 2 forms, bullous and non-bullous variants. Infection can either be **Primary impetigo**: Bacterial infection of previously healthy skin, intact and **Secondary impetigo** (impetiginization): Secondary infection of pre-existing skin lesions/abrasions.
- Epidemiology: Primarily affects children (especially age between 2 to 6 years of age). Impetigo is highly contagious and can cause epidemics in preschools or schools.
- Predisposing factors: Warm and humid climate, Crowded, unsanitary living conditions, Poor personal hygiene, medical conditions, Pre-existing skin lesions (e.g., atopic dermatitis, scabies, insect bites, abrasions, eczema), Diabetes mellitus, Immunodeficiency (e.g., HIV, post-organ transplantation, systemic corticosteroids).

CLINICAL PRESENTATION OF IMPETIGO (MOST COMMON)

Non-bullous impetigo = 70% of cases		Bullous impetigo = 30% of cases
Features		
Lesions on physical examination	» Papules, which turn into small vesicles surrounded by erythema and/or pustules. ▪ Vesicles and pustules can rupture. ▪ Oozing secretion that dries forms honey-colored crusts that heal without scarring. » May be pruritic (especially pustules) but is rarely painful. » Negative Nikolsky sign	» Vesicles that grow to form large, flaccid bullae, which go on to rupture and form thin, brown crusts. » Bullae are fluid-filled lesions >0.5 cm in diameter. » Negative Nikolsky sign
Distribution pattern	» Face (most common), especially around the nose & mouth » Extremities	» Trunk and upper extremities
Other findings	» Regional lymphadenopathy	» In severe cases: fever, malaise, weakness

- Ecthyma (Rare manifestation)
 - » Ulcerative impetigo that extends into the dermis
 - » Manifests as a coin-sized, superficial ulcer with a punched-out appearance
- Complications of impetigo: include post-streptococcal glomerulonephritis, cellulitis, and scarlet fever

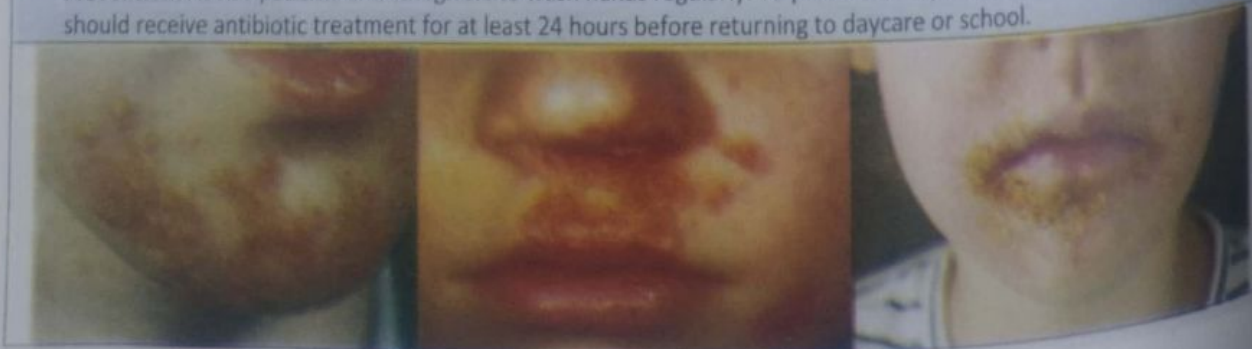
DIAGNOSTIC APPROACH OF IMPETIGO

- Generally diagnosed based on clinical presentation.
- Clinical History and Examination
 - » Key Factors: Vesicles/bullae, crusting (usually presents a classic facial yellowish to golden crusting)
 - » Other Factors: Erythema, pruritus, pain, mucopurulent exudate, lymphadenopathy, and fever
- Investigation Positive Gram stain and **Positive Bacterial skin culture** (superficial wound culture) → Indications of skin culture: if the diagnosis is in doubt, or if the patient fails to respond to appropriate empiric therapy for impetigo.



TREATMENT OF IMPETIGO

- General: Skin hygiene, Wound cleansing with antibacterial washes, and do not share towels or face cloths.
- Mild non-bullous impetigo: single lesions or small areas affected → **Topical antibiotics** (Mupirocin/Fusidic acid)
 - » Mupirocin 2% ointment (Bactroban, Mupir) x Apply topically to the affected area, 2 – 3 times daily for 7 days.
 - » OR Fusidic acid 2% cream (Fudic, Fuciderm, Fucidin) x Apply topically to the affected area, twice daily for 5 days.
- Bullous impetigo/Ecthyma/Severe non-bullous impetigo: Widespread dispersion, numerous lesions, &/or fever
 - » First-line treatment: First generation cephalosporins (e.g., cephalexin, Cefadroxil) or dicloxacillin/flucloxacillin
 - » Syp. Cephalexin (Ceporex, Keflex 125mg/5ml OR 250mg/5ml) at dose 25-50mg/kg/day x BD/TDS
 - » OR Syp. Cefadroxil (Duricef, Cedrox 125mg/5ml OR 250mg/5ml) at dose 30mg/kg/day divided every 12 hourly
 - » OR Syp. Co-amoxiclav (Augmentin) child <3months 30mg/kg/day x BD, > 3months <40kg 30-90mg/kg/day x TDS
 - » If MRSA infection; is confirmed or suspected: Clindamycin, Co-trimoxazole (Septran), Vancomycin
- Prevention: Advise patients and caregivers to wash hands regularly. To prevent the spread of the disease, children should receive antibiotic treatment for at least 24 hours before returning to daycare or school.



DOG BITE (RABIES VIRUS) IN CHILDREN

THREE CATEGORIES OF DOG BITES EXPOSURE BY WHO

- Category I: Touching/Feeding of animals, Licks on intact skin (No risk of infection if the history is reliable).
- Category II: Nibbling of uncovered skin or minor scratches or abrasions without bleeding (Low risk of infection).
- Category III: Single or multiple transdermal bites or scratches, licks on broken skin, contamination of mucous membrane with saliva from licks, or exposure to bat bites or scratches (High risk of infection).

POST-EXPOSURE PROPHYLAXIS (PEP) – GUIDELINES

- Category II and III exposures require post-exposure prophylaxis (PEP)
- Wound care: immediately extensive washing of the wound with water and soap for at least 15 minutes and local treatment of the wound as soon as possible after a suspected exposure.
- The WHO recommends either an intradermal/ID (3-dose) or intramuscular/IM (4-dose or 2-1-1 dose) regimen.
- The intradermal (ID) regimen is preferred, as this reduces the amount of necessary vaccine and therefore the cost by 60-80% without compromising any safety or efficacy and time-sparing regimen.
- The Advisory Committee on Immunization Practices (ACIP): The Rabies vaccine (1 dose) is given on days 0, 3, 7, and 14 (an additional dose at 28 days is recommended if the patient is immunocompromised) x intramuscular (IM).
- Site of injection: intramuscular injection is given into the deltoid area in children's ≥ 2 (in children 2 years or more than 2 years of age) and anterolateral area of the thigh is recommended for children aged less than 2 years
- PEP does not have any contraindications, if purified rabies immunoglobulin & rabies vaccine are used. It is recommended in children and pregnant women. If repeat exposure occurs within 3 months of PEP, further PEP is not required
- Asymptomatic patients with recent vector exposure (Symptomatic rabies is rare, and almost always fatal).
- Unimmunized: non-bite exposure with no infection risk → Reassurance, no risk of infection, treatment not required
- Unimmunized: non-bite exposure with low infection risk → wound treatment, rabies vaccine and immunoglobulin.
- Unimmunized: bite exposure, licks on broken skin or mucous membrane, or exposure to bat bites or scratches → wound treatment, rabies vaccine and rabies immunoglobulin.
- Immunized: any exposure with infection risk → even patients who have been vaccinated against rabies should be treated after exposure! No immunoglobulin. Check antibody titers on day 14.



TREATMENT OF DOG BITES

- Wound management: The wound should be thoroughly washed and flushed with soap and water (or water alone) for 15 minutes, and disinfected immediately with detergent, iodine (tincture), or ethanol (700ml/l).
- POST-EXPOSURE PROPHYLAXIS (PEP)
 - Multiple-dose rabies vaccine (immunization) protocol
 - Un-immunized patient: Rabies vaccine (Inj. Verorab 0.5ml, Inj. Indirab 0.5ml, Inj. Rabipur 1.0ml)
Dosage: One I/M dose = 0.5ml or 1ml, One I/D dose = 0.1ml, depending on the vaccine manufacturer
 - WHO protocols: Intradermal (3-dose) or intramuscular (4-dose) or (4-dose or 2-1-1 dose) regimen.
 - Rabies vaccine at dose 0.1mL (divided between 2 sites) on days 0, 3, and 7 x intradermally (I/D)
 - OR Rabies vaccine 1 dose (at 1-site) on days 0, 3, 7, and between days 14-28 x intramuscular (I/M)
 - ACIP protocol: Rabies vaccine (Inj. Verorab 0.5ml, Inj. Indirab 0.5ml) on days 0, 3, 7, and 14 (and 28 in immunocompromised patients) x intramuscular (IM)
 - Immunized patient:
 - WHO protocols: Rabies vaccine 0.1 mL, 1 dose on days 0 and 3 x ID/IM
 - ACIP protocol: Rabies vaccine 0.5 mL or 1 mL on days 0 and 3 x intramuscularly (IM)
- Rabies immunoglobulin: HRIG 300 I.U./2ml (HyperRAB, Imogam rabies-HT, Berirab-P) OR ERIG 1000 I.U./5ml (Equirab) is given into the site of the wound by intramuscular (IM) injection
 - Human rabies immunoglobulin (HRIG) at dose 20 IU/kg (0.133 ml/kg)

➤ Patient weight 30kg x 20 I.U. = 600 I.U.	➤ 600 ÷ 150 I.U./ml = 4 ml
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 - Equine rabies immunoglobulin (ERIG): at dose 40 IU/kg (0.200 ml/kg)

➤ Patient weight 30kg x 40 I.U. = 1200 I.U.	➤ 1200 ÷ 200 I.U./ml = 6 ml
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- Tetanus prophylaxis: Inj. Imatet 0.5ml x IM x STAT, repeat after 4 weeks as per protocol and vaccination history
- Analgesia for pain control: Inj. Ketorolac 30mg/ml at dose 15-30mg x IV/IM OR oral as mentioned below
- Counsel the patient and discharge on analgesia ± antibiotics if indicated
 - Syp. Co-Amoxiclav (Augmentin, Amclav) x BD OR Syp. Cefixime 200mg/5ml (Cefspan DS, Cefim DS) x OD
 - Syp. Paracetamol 250mg/5ml (Calpol 6 Plus, Panadol forte) at dose 15mg/kg/dose x TDS/QID. Max 75 mg/kg/day
 - OR Syp. Ibuprofen (Brufen= 100mg/5ml, Brufen DS= 200mg/5ml) at dose 10mg/kg/dose x TDS/QID.

TETANUS

CLINICAL FEATURES

- ☞ Occurs in infants of inadequately immunized mothers after unsterile management of the umbilical stump.
- ☞ **Incubation period:** Typically occurs 3–10 days after birth, but the incubation period can take up to several weeks
- ☞ Typically, a rapid onset of symptoms as axonal length in infants is shorter than in adults
- ☞ **Symptoms**
 - » Febrile, Irritability, Heavy sweating
 - » **Generalized tetanus:** painful muscle spasms and muscle rigidity
 - » Difficulty opening the mouth and poor sucking due to **trismus (lock jaws)** and **risus sardonicus** (a characteristic, apparently sardonic grin and raised eyebrows) due to sustained tetanic spasms of the facial muscles.
 - » **Opisthotonus** (backward arching of spine, neck, and head caused by spasms of the back muscles)
 - » Neck stiffness, clenched hands and abdominal rigidity
 - » Other features: dysphagia, apnea, asphyxia, cyanosis, tachycardia
- ☞ **Risk factors:** Contaminated wound, home delivery, un-vaccinated mother, umbilical cord cutting with unsterilized instrument, and traumatic injury with unsterilized object
- ☞ **Life-threatening complications**
 - » Laryngospasm and/or respiratory muscles spasms → respiratory failure
 - » Autonomic dysfunction → circulatory arrest and shock.

DIAGNOSTIC WORKUP

- ☞ Diagnosis of tetanus is primarily based on clinical features and further testing is usually not necessary.
- ☞ **Clostridium tetani:** may be detected in the infection site by direct PCR & strict anaerobic culture of wound tissue/swabs.
- ☞ Tetanus toxin can be detected in serum, confirming a clinical diagnosis, but low sensitivity and specificity

TREATMENT OF TETANUS



Principles of management: 1. Eradication of clostridium tetani. 2. Neutralization of tetanus toxin. 3. Control of seizures and respiration. 4. Palliation and provision of supportive care. 5. Prevention of recurrences.

- ☞ Stabilize patient with ABCD&E approach
- ☞ Establish intravenous (IV) access
- ☞ Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂ (Give high flow O₂ as appropriate, if SpO₂ <94%)
- ☞ Isolate and Keep the Patient in dark quiet room.
- ☞ Pass nasogastric (NG) tube, keep child NPO, N.B. Don't insert nasogastric tube unless the patient is fully sedated.
- ☞ IV fluid therapy, Maintenance of fluid and correction of electrolyte imbalance
- ☞ Wound debridement: All wounds should be thoroughly debrided. Wound debridement removes spores and necrotic tissue after giving HTIG, eradicating the anaerobic conditions that facilitate clostridial growth.
- ☞ Removal of umbilical stump in neonate is not recommended.
- ☞ Human tetanus immunoglobulin (HTIG) to neutralize the toxin: Inj. TIG 250 I.U x I.M. once
 - ☞ If not available tetanus equine antitoxin in dose of 50,000–100,000 U I.M (Check for sensitivity is needed).
- ☞ Inj. Tetanus toxoid vaccine (Imatet) x IM on arm (Inject in a separate site from HTIG) ^{HTIG = human tetanus immunoglobulin}
- ☞ Start antibiotics therapy
 - » Drug of choice: Inj. Metronidazole 500mg/100ml (Flagyl) at dose 15mg/kg/dose over 30minute, followed by 7.5mg/kg x 8 to 12 hours for 7 to 10 days
 - » Alternative: Inj. Penicillin-G 1.2 million units/vial (Benzibiotic), was historically used, but is no longer favorable due to GABA antagonism (potentiates tetanospasmin, worsening muscle rigidity and spasms).
 - Children > 28 days old (FDA-approved only if > 20 kg): 100,000–300,000 units/kg/day IV/IM divided equally every 4–6 hours for 7–10 days (max. daily dose 24 million IU)
 - Neonates 7–28 days old (off-label): 150,000 units/kg/day IV/IM divided equally every 8 hours for 7–10 days
 - Neonates < 7 days old (off-label): 100,000 units/kg/day IV/IM divided equally every 12 hours for 7–10 days
 - » OR secondary option: Inj. Vancomycin at dose 15 to 20 mg/kg every 8 to 12 hours
- ☞ For seizure/relaxation: Inj. Diazepam 10mg/2ml (Valium) at dose 0.1–0.2mg/kg every 3–6 hr IV for 2–5 weeks.
- ☞ Gastroprotective: Inj. Esomeprazole 40mg/vial (Nexum) at dose 0.5 mg/kg/dose once daily (10–20mg x OD).
- ☞ Tetanus with severe muscle spasms: Vecuronium or Rocuronium or intrathecal baclofen
- ☞ Tetanus with autonomic dysfunction: Magnesium sulphate and morphine sulphate and Labetolol
- ☞ Careful nursing to mouth, skin, bladder, and bowel function is needed to avoid ulceration and infection



IMMUNIZATION SCHEDULE IN CHILDREN'S

WHEN TO GIVE	VACCINE	DOSE	ROUTE
At birth	1. BCG ↳ Bacillus Calmette–Guérin	<3 months: 0.05ml > 3months: 0.1ml	Intradermal at Left upper arm (preferred deltoid)
	2. OPV (Poliovirus)-0	2 drops	Per orally
	3. Hepatitis-B (HB)		
6 weeks	1. Diphtheria-Pertussis-Tetanus (DPT), Hepatitis-B, Hemophilus influenza type-B ↳ Pentavalent (DPT + Hib + Hep-B) – 1	0.5ml	Intramuscular, Anterolateral side of mid-thigh
	2. OPV (Poliovirus)-1	2 drops	Per orally
	3. Pneumococcal Conjugate vaccine (PCV)-1	0.5ml	Intramuscular
	4. Rotavirus vaccine (RV)-1	1ml	Per orally
10 weeks	1. Diphtheria-Pertussis-Tetanus (DPT), Hepatitis-B, Hemophilus influenza type-B ↳ Pentavalent (DPT + Hib + Hep-B) – 2	0.5ml	Intramuscular, Anterolateral side of mid-thigh
	2. OPV (Poliovirus)-2	2 drops	Per orally
	3. Pneumococcal Conjugate vaccine (PCV)-2	0.5ml	Intramuscular
	4. Rotavirus vaccine (RV)-2	1ml	Per orally
14 weeks	1. Diphtheria-Pertussis-Tetanus (DPT), Hepatitis-B, Hemophilus influenza type-B ↳ Pentavalent (DPT + Hib + Hep-B) – 3	0.5ml	Intramuscular, Anterolateral side of mid-thigh
	2. OPV (Poliovirus)-3	2 drops	Per orally
	3. Pneumococcal Conjugate vaccine (PCV)-3	0.5ml	Intramuscular
	4. Inactivated polio vaccine (IPV)-1		
9 months	1. Inactivated polio vaccine (IPV)-2	0.5ml	Intramuscular at Anterolateral side of mid-thigh OR Subcutaneous at Upper arm
	2. Typhoid	0.5ml	Intramuscular
	3. Measles, Mumps, Rubella (MMR)-1	0.5ml	Subcutaneous
15 months	1. Measles, Mumps, Rubella (MMR)-2	0.5ml	Subcutaneous
> 2 years	1. Typhoid	0.5ml	Intramuscular
	2. Varicella vaccine (VAR)/chickenpox	0.5ml	Subcutaneous
	3. Meningococcal conjugate vaccine (MCV)	0.5ml	Intramuscular
Upto 5 years	1. OPV (Poliovirus)	2 drops	Per orally

IV PAEDIATRICS DOSAGES QUICK CHART

GENERIC NAME	BRAND NAME	DOSE
Ampicillin	Inj. Zampicillin 500mg Inj. Zampicillin 1g	Neonates: 50 mg/kg every 6-12 hrs. Infants & children: 100-200 mg/kg/day divided every 6 hours.
Amoxicillin/clavulanate potassium (Co-Amoxiclav)	Inj. Augmentin 0.6g /vial OR 1.2g/vial Inj. Calamox 0.6g /vial OR 1.2g/vial	Infants & children: 30 mg/kg/day of amoxicillin divided every 8-12 hours.
Piperacillin + Tazobactam	Inj. Tanzo 2.25g/vial Inj. Tanzo 4.5g/vial	Infants & children: 100 mg/kg of piperacillin x TDS (every 8 hours)
Imipenem/ Cilastatin	Inj. Tienam 500mg/vial Inj. Claforan 0.5g/vial Inj. Claforan 1g/vial	Infants & children: 15-25 mg/kg x QID Neonates: 50 mg/kg every 12 hours. Infants & children: 100-200 mg/kg per day divided every 6-8 hours.
Cefotaxime	Inj. Oxidil 500mg/vial or 1g/vial Inj. Rocephin 500mg/vial or 1g/vial	Neonates: 50 mg/kg once daily (OD) Infants & children: 50-75 mg/kg x OD
Ceftazidime	Inj. Fortum 500mg/vial Inj. Fortum 1g/vial	Infants & children: 100-150 mg/kg/day divided every 8 hours.
Cefuroxime	Inj. Zinacef 750mg/vial Inj. Zinacef 1.5g/vial	Infants & children: 75-150 mg/kg/day divided every 6-8 hours.
Cefoperazone	Inj. Cefobid 1g/vial Inj. Cefobid 2g/vial	Infants & children: 100-200 mg/kg/day divided every 12 hours.
Cefazolin	Inj. Kefzol 500mg/vial Inj. Kefzol 1g/vial	Infants & children: 50-100 mg/kg/day divided every 6-8 hours.
Cefepime	Inj. Uceph 1g/vial Inj. Uceph 2g/vial	Infants & children: 50 mg/kg every 8-12 hours.
Azithromycin	Inj. Azitma 500mg/vial Inj. Zerot 500mg/vial	Infants & children: 10 mg/kg on day 1, followed by 5 mg/kg x OD for 4 days
Clarithromycin	Inj. Klaricid 500mg/vial Inj. Rithmo 500mg/vial	Infants & children: 7.5 mg/kg every 12 hours (BD).
Lincomycin	Inj. Lincocin 300mg/1ml Inj. Lincocin 600mg/2ml	Infants & children: 10-20 mg/kg every 8-12 hours.
Clindamycin	Inj. Dalacin-C 300mg/2ml Inj. Dalacin-C 600mg/4ml	Infants & children: 10-20 mg/kg/day divided every 6-8 hours.
Ofloxacin	Inj. Tariflox 200mg/100ml	Infants & children: 7.5-15 mg/kg x BD
Ciprofloxacin	Inj. Novidat 200mg/100ml	Infants & children: 10-20 mg/kg every 12 hours.
Levofloxacin	Inj. Leflox 500mg/100ml	Infants & children: 10 mg/kg every 12-24 hours.
Amikacin	Inj. Amkay OR Inj. Grasil 50mg, OR 100mg, 250mg, OR 500mg	Neonates: 15 mg/kg once daily. Infants & children: 15-20 mg/kg once daily or divided every 8-12 hours.
Gentamicin Sulfate	Inj. Gentamicin 40mg/1ml	Neonates: 4-5 mg/kg once daily. Infants & children: 2.5mg/kg every 8 hrs
Vancomycin	Inj. Vancomycin 500mg/vial Inj. Vancomycin 1g/vial	Neonates: 15 mg/kg every 12 hours. Infants & children: 15 mg/kg every 6-8 hours.
Linezolid	Inj. Nezkil 600mg/300ml	Infants & children: 10 mg/kg every 8 hours.
Meropenem	Inj. Meronem 500mg/vial OR 1g/vial	Neonates: 20 mg/kg every 8-12 hours. Infants & children: 20-40 mg/kg every 8 hours.





Metronidazole	Inj. Flagyl 500mg/100ml	Infants & children: 7.5 mg/kg every 8 hours.
Paracetamol	Inj. Provas 1g/100ml	Infants & children: 10-15 mg/kg every 4-6 hours.
Ibuprofen	Inj. Inbufin 400mg/100ml	Infants & children: 5-10 mg/kg every 6-8 hours.
Ketorolac Tromethamine	Inj. Toradol 30mg/ml	Children > 2 years: 0.5 mg/kg x TDS
Dimenhydrinate	Inj. Gravinate 50mg/1ml	Infants & children: 0.5-1mg/kg every 6-8 hours.
Metoclopramide	Inj. Metaclon 10mg/2ml	Infants & children: 0.1-0.15 mg/kg every 6-8 hours.
Ondansetron	Inj. Onset 8mg/4ml	Infants & children: 0.1mg/kg (up to 4 mg) every 8 hours.
Granisetron	Inj. Graniset 3mg/3ml	Infants & children: 10 mcg/kg x OD
Drotaverine	Inj. Nospa 40mg/2ml	0.5-1mg/kg/day (NOT recommended)
Omeprazole	Inj. Risek 40mg/vial	Infants & children: 0.5-1 mg/kg x OD
Acyclovir	Inj. Acyclovir 500mg/10ml/vial	Neonates: 20mg/kg every 8 hours (TDS) Infants & children: 10 mg/kg x TDS
Pheniramine Maleate	Inj. Avil 50mg/2ml	Infants & children: 0.5-1 mg/kg every 6 hours.
Diazepam	Inj. Valium 10mg/2ml	Infants & children: 0.1-0.2 mg/kg every 6-8 hours.
Midazolam	Inj. Dormicum 5mg/5ml	Infants & children: 0.05-0.1 mg/kg every 2-4 hours as needed.
Phenobarbitone	Inj. Phenobarb 200mg/2ml	Neonates: 15-20 mg/kg loading dose, then 5 mg/kg once daily (OD). Infants & children: 3-5 mg/kg x OD
Valproate Sodium	Inj. Epival 500mg/5ml	Infants & children: 10-15 mg/kg/day divided every 8-12 hours.
Levetiracetam	Inj. Lerace 500mg/5ml	Infants & children: 10-20 mg/kg every 12 hours.
Phenytoin	Inj. Epigran 250mg/5ml	Neonates: 15-20 mg/kg loading dose, then 5-8 mg/kg/day x BD Infants & children: 5-8 mg/kg/day divided every 8-12 hours.
Furosemide	Inj. Lasix 20mg/2ml	Neonates: 0.5-1 mg/kg every 12-24 hours. Infants & children: 1-2 mg/kg every 6-12 hours.
Hydrocortisone	Inj. Solu-Cortef 100mg/vial Inj. Solu-Cortef 250mg/vial	Infants & children: 2-4 mg/kg/day divided every 6 hours.
Methylprednisolone Sodium Succinate	Inj. Solu-Medrol 125mg/2ml Inj. Solu-Medrol 500mg/vail	Infants & children: 1-2 mg/kg/day divided every 6-12 hours.
Atropine	Inj. Atropine 1mg/1ml	Infants & children: 0.01-0.02 mg/kg every 4-6 hours as needed.
Fluconazole	Inj. Diflucan 2mg/1ml (100mg/50ml)	Infants & children: 6-12 mg/kg once daily.
Labetalol	Inj. Labetalol 50mg/10ml (5mg/ml)	Infants & children: 0.2-1 mg/kg per dose every 6-8 hours.
Insulin (Regular)	Inj. Humulin-R 100IU/ml Inj. Insuget 100IU/ml	Infants & children: 0.1-0.2 units/kg/dose every 4-6 hours, adjust based on blood glucose levels.

ORAL PAEDIATRICS DOSAGES QUICK CHART

GENERIC NAME	BRAND NAME	DOSE
Paracetamol	Syp. Calpol 120mg/5ml Syp. Calpol 6 plus 250mg/5ml	Infants & children: 10-15 mg/kg every 4-6 hours (maximum 75 mg/kg/day).
Ibuprofen	Syp. Brufen 100mg/5ml Syp. Brufen DS 200mg/5ml	Infants & children: 5-10 mg/kg every 6-8 hours (maximum 40 mg/kg/day).
Dexibuprofen	Syp. Tercica 100mg/5ml Syp. Dexibu 100mg/5ml	Infants & children: 5-10 mg/kg every 6-8 hours (maximum 30 mg/kg/day).
Mefenamic Acid	Syp. Ponstan 50mg/5ml Syp. Ponstan fort 100mg/5ml	Children ≥6 months: 6.5 mg/kg every 6-8 hours. (maximum 25 mg/kg/day)
Ampicillin	Syp. Penbritin 125mg/ml Cap. Penbritin 250mg Cap. Penbritin 500mg	Neonates: 50 mg/kg every 6-12 hrs. Infants & children: 100-200 mg/kg/day divided every 6 hours.
Amoxicillin	Syp. Amoxil 125mg/5ml Syp. Amoxil 250mg/5ml	Infants & children: 25-50 mg/kg/day divided every 8-12 hours.
Amoxicillin/clavulanate potassium (Co-Amoxiclav)	Syp. Augmentin 156.25mg/5ml, Syp. Augmentin DS 312.50/5ml Syp. Augmentin BD 457mg/5ml Augmentin infant drops 62.5mg/1ml	Infants & children: 20-40 mg/kg/day of amoxicillin divided every 8-12 hours.
Cefadroxil	Syp. Duricef 125mg/5ml Syp. Duricef 250mg/5ml	Infants & children: 30 mg/kg/day divided every 12 hours.
Cefaclor	Syp. Ceclor 125mg/5ml Syp. Ceclor 187mg/5ml Syp. Ceclor 250mg/5ml Ceclor 50mg/1ml infant drops	Infants & children: 20-40 mg/kg/day divided every 8-12 hours.
Cephalexin	Syp. Ceporex 125mg/5ml Syp. Ceporex 250mg/5ml Ceporex 100mg/1ml infant drops	Infants & children: 25-50 mg/kg/day divided every 6-12 hours.
Cefuroxime Axetil	Syp. Zecef 125mg/5ml Syp. Evorox 125mg/5ml	Infants & children: 20-30 mg/kg/day divided every 12 hours.
Cefixime	Syp. Cefspan 100mg/5ml Syp. Cefspan DS 200mg/5ml	Infants & children: 8 mg/kg/day once daily or divided every 12 hours.
Cefpodoxime	Syp. Abacus 40mg/5ml Syp. Abacus 100mg/5ml	Infants & children: 10 mg/kg/day divided every 12 hours.
Clindamycin	Cap. Dalacin-C 150mg Cap. Dalacin-C 300mg	Infants & children: 8-25 mg/kg/day divided every 6-8 hours.
Erythromycin	Syp. Erythrocin 100mg/5ml Syp. Erythrocin 200mg/5ml	Infants & children: 30-50 mg/kg/day divided every 6-8 hours.
Azithromycin	Syp. Azitma 200mg/5ml Syp. Azomax 200mg/5ml	Infants & children: 10 mg/kg on day 1, then 5 mg/kg once daily for 4 days.
Clarithromycin	Syp. Klaricid 125mg/5ml Syp. Klaricid 250mg/5ml	Infants & children: 7.5 mg/kg every 12 hours.
Lincomycin	Syp. Lincocin 250mg/5ml Syp. Omicin 250mg/5ml	Infants & children: 30-60 mg/kg/day divided every 6-8 hours.





Ciprofloxacin	Syp. Novidat 125mg/5ml Syp. Novidat 250mg/5ml	Infants & children: 10-15 mg/kg every 12 hours (max 750 mg/dose).
Trimethoprim + Sulfamethoxazole (Co-Trimoxazole)	Syp. Septran 40mg/200mg Syp. Septran DS 80mg/400mg	Infants & children: 6-12 mg/kg/day (based on trimethoprim component) divided every 12 hours.
Linezolid	Syp. Nezkil 100mg/5ml Syp. Nezocin 100mg/5ml	Infants & children: 10 mg/kg every 8-12 hours.
Metronidazole	Syp. Flagyl 200mg/5ml Syp. Klint 200mg/5ml	Infants & children: 7.5 mg/kg every 8 hours.
Nitazoxanide	Syp. Izato 100mg/5ml Syp. NT-Tox 100mg/5ml	Infants (1-3 years): 100 mg every 12 hours. Children (4-11 years): 200 mg every 12 hours.
Acyclovir	Syp Acylex 200mg/5ml Tab. Acylex 200mg and 400mg	Infants & children: 20 mg/kg every 8 hours.
Chloroquine	Syp. Nivaquine-P 50mg/5ml Tab. Nivaquine-p 250mg	Infants & children: 10 mg/kg on day 1, then 5 mg/kg on days 2 and 3.
Pyrimethamine and Sulphadoxine	Syp. Fansidar 500mg/25mg per 15ml Tab. Fansidar 500mg/25mg	Infants & children: Single dose of 1.25 mg/kg pyrimethamine and 25 mg/kg Sulfadoxine.
Fluconazole	Syp. Fonaz 50mg/5ml	Infants & children: 6-12 mg/kg once daily.
Nystatin	Nilstat 100,000 units/1ml Myconil 100,000 units/1ml	Infants & children: 100,000 units 4 times daily (oral suspension).
Domperidone	Syp. Motilium 5mg/5ml Syp. Domel 5mg/5ml	Infants & children: 0.2-0.3 mg/kg every 6-8 hours.
Dimenhydrinate	Syp. Gravinate 12.5mg/4ml	Infants & children: 1 mg/kg every 6 hours (max 300 mg/day).
Metoclopramide	Syp. Maxolon 5mg/ml Syp. Metaclon 5mg/ml	Infants & children: 0.1-0.15 mg/kg every 6-8 hours.
Ondansetron	Syp. Onseron 4mg/5ml Syp. Onset 4mg/5ml	Infants & children: 0.15 mg/kg (up to 8 mg) every 8 hours.
Albendazole	Syp. Zentel 200mg/5ml (400mg/10ml) Syp. Bendazole 200mg/5ml	Infants (12-24 months): 200 mg once. Children (>2 years): 400 mg once.
Mebendazole	Syp. Vermox 20mg/1ml (100mg/5ml) Tab. Vermox 100mg Tab. Vermox 500mg	Children (≥ 2 years): 100 mg twice daily for 3 days or 500 mg once.
Levamisole	Syp Ketress 40mg/5ml Tab Ketress 40mg	Children: 2.5 mg/kg once.
Pheniramine Maleate	Syp. Avil 15mg/5ml Tab. Avil 25mg	Infants & children: 1 mg/kg/day divided every 6-8 hours.
Chlorpheniramine Maleate	Syp. Piriton 2mg/5ml Tab. Piriton 4mg	Infants (1-2 years): 1 mg twice daily. Children (2-5 years): 1 mg every 6 hours Children (>6 years): 2 mg every 6 hours
Cetirizine	Syp. Rigix 5mg/5ml Rigix infants drops 10mg/ml Tab. Rigix 10mg	Infants (6-23 months): 2.5 mg x OD Children (2-5 years): 2.5-5 mg x OD Children (>6 years): 5-10 mg x OD

Loratadine	Syp. Softin 5mg/5ml Syp. Lorin NSA 5mg/5ml	Infants (2-5 years): 5 mg x OD Children (>6 years): 10 mg x OD
Desloratadine	Syp. Desora 0.5mg/1ml Syp. Neo-Antial 0.5mg/1ml Syp. Jordin-D 0.5mg/1ml	Infants (6-11 months): 1 mg once daily. Children (1-5 years): 1.25 mg once daily. Children (6-11 years): 2.5 mg once daily. Children (>12 years): 5 mg once daily.
Hyoscine butylbromide	Syp. Gravinate 12.5mg/4ml	Children: 0.3-0.6 mg/kg every 6-8 hours.
Acetazolamide	Tab. Diamox 250mg Tab. AZM 250mg	Infants & children: 5-10 mg/kg/day divided every 8-12 hours.
Furosemide	Tab. Lasix 20mg Tab. Lasix 40mg	Infants & children: 1-2 mg/kg every 6-12 hours.
Salbutamol	Syp. Ventolin 2mg/5ml Syp. Bronkal 2mg/5ml	Infants & children: 0.1-0.15 mg/kg every 4-6 hours.
	Syp. Britanyl 0.3/ml Syp. Tesmic 0.3mg/ml	Infants & children: 0.05 mg/kg/dose every 8 hour (Maximum 5 mg).
Montelukast	Tab. Myteka 4mg, Tab. Mytika 5mg Myteka sachets 4mg Myteka sachets 5mg	Infants (6-23 months): 4 mg once daily. Children (2-5 years): 4 mg once daily. Children (6-14 years): 5 mg once daily.
Prednisolone	Syp. Rapicort 5mg Tab. Rapicort 5mg	Infants & children: 1-2mg/kg/day X OD/BD (maximum 60 mg/day).
Dexamethasone	Tab. Kanadex 0.5mg Tab. Oradexon 0.5mg	Infants & children: 0.15-0.6 mg/kg/day divided every 6-12 hours.
Phenobarbitone	Syp. Debritone 20mg/5ml Tab. Phenobarbitone 30mg	Infants & children: 3-5 mg/kg/day once daily.
Valproate Sodium	Syp. Epival 250mg/5ml Syp. Dapakan 200mg/5ml,	Infants & children: 10-15 mg/kg/day divided every 8-12 hours.
Levetiracetam	Syp. Lerace 100mg/1ml Syp. Eplipsa 100mg/1ml	Infants & children: 10-20 mg/kg twice daily.
Phenytoin	Syp. Epitoin 125mg/5ml Syp. Dilantin 125mg/5ml	Infants & children: 5-8 mg/kg/day divided every 8-12 hours.
Famotidine	Syp. Polypep 10mg/5ml Syp. Famot 10mg/5ml	Infants & children: 0.5 mg/kg once daily.
Omeprazole	Cap. Ruling 20mg Cap. Risek 20mg	Infants & children: 0.5-1 mg/kg once daily.
Lactulose	Syp. Duphalac Syp. Lilac	Infants & children: 1-3 mL/kg/day divided 1-2 times daily.
Vitamin D	Sunplex-D drops 400IU D-Max drops 400IU	Infants: 400 IU once daily. Children: 600-1000 IU once daily.
Iron (Ferrous Sulfate)	Syp. IBERET (Iron per 5ml = 26.25mg)	Infants & children: 3-6 mg/kg/day divided every 8-12 hours.

Note: These dosages are general guidelines and should be confirmed with current clinical guidelines and individual patient factors. Always consult a healthcare professional before administering any medication.

THE PRIMARY, SECONDARY & TERTIARY SURVEYS

- » In this station, you are going to be asked to assess a patient with a medical emergency or who has suffered severe trauma (e.g. from a road traffic accident).
- » What follows is a general outline of the areas that you are going to need to cover.

PRIMARY SURVEY

THE QUICK LOOK

- » Inspect (look) the patient.
- » Introduce yourself to him.
- » Is he responsive? Try to elicit a response by shouting out his name.

AIRWAY & CERVICAL SPINE

- » Assess the airway for obstruction.
- » If necessary, clear, and secure the airway.
- » If there is suspicion of a cervical spine injury, use the jaw-thrust technique.
- » If there is suspicion of cervical spine injury, immobilize the cervical spine in a stiff collar.
- » Place sandbags on either side of the head and tape them across the forehead.

BREATHING

- » **Assess breathing:** look, listen, feel.
- » Expose the chest.
- » Note the rate and depth of respiration.
- » Look for asymmetries of chest expansion.
- » Look for chest injuries.
- » Palpate for tracheal deviation. Palpate, percuss, and auscultate the chest. Try to exclude flail segments, pneumothorax, or haemothorax.
- » Attach a pulse oximeter.
- » If appropriate, ventilate using a bag, mask, and oropharyngeal airway or endotracheal tube.

CIRCULATION & HAEMORRHAGE CONTROL

- » Control any visible haemorrhage by direct pressure.
- » **Look for clinical signs of shock:** Assess the pulse, skin colour, capillary refill time, JVP, heart sounds, and blood pressure. Try to exclude cardiac tamponade.
- » Attach an ECG monitor.
- » Establish TWO large-bore (Grey) cannulas into large peripheral veins.
- » Take a sample of blood for group and crossmatch.
- » Start IV fluid replacement.

DISABILITY (NEUROLOGICAL ASSESSMENT)

- » **Assess neurological function on the AVPU scale:**
 - ↳ Alert
 - ↳ Voice elicits a response
 - ↳ Pain elicits a response
 - ↳ Unresponsive
- » Assess the pupils for size and reactivity.
- » Check that all limb extremities can be moved.

EXPOSURE AND ENVIRONMENTAL CONTROL

- » Remove the patient's remaining clothing and inspect both his front and back. Log-roll him (with the help of others) so that his spine remains immobilized.
- » Cover him with a blanket.

SECONDARY SURVEY & TERTIARY SURVEY

ONCE THE PATIENT IS STABLE:

- Take a short, AMPLE history:
 - » Allergies
 - » Medications and tetanus immunity
 - » Previous/past medical history, Pregnancy
 - » Last meal
 - » Events related to injury
- Carry out a head-to-toe systemic assessment of abdominal, pelvic & thoracic areas
- Complete inspection of body surface to find all injuries & neurological examination
- Monitor ECG, BP, oxygen saturation, Bed side RBS and core temperature.
- Insert a urinary catheter and, if necessary, a nasogastric tube (to aspirate stomach contents).
- **Order investigations:** CBC, BUN/urea, creatinine, electrolytes, liver function tests, amylase, blood glucose, coagulation profile, arterial blood gases (ABGs), toxicology screen,
- **Radiology:**
 - » X-rays of the lateral cervical spine, chest and pelvis.
 - » If indicated CT scan based on examination finding.
- Encourage questions from the patient and address his concerns.

FAST (= FOCUSED ASSESSMENT WITH SONOGRAPHY FOR TRAUMA)

- FAST: Emergency ultrasound done very fast, performed within 2 – 4 minutes
- Rapid diagnostic examination to assess patients with potential thoraco-abdominal injuries.
- FAST is the first investigation done in blunt trauma abdomen; FAST has replaced DPL.
- **Traditional standard '4' views of FAST: 4 'P's are evaluated in the sequence:** 1. Pericardial sac assess at Subxiphoid transverse view → Perihepatic region assess at Right upper quadrant (RUQ) longitudinal view → Perisplenic region assess at Left upper quadrant (LUQ) longitudinal view → Pelvis assess at Suprapubic longitudinal & transverse view.
- e-FAST (extended FAST) has two additional views, right thoracic views and left thoracic views to rule out pneumothorax or hemothorax.

FAST VS E-FAST

Detection of blood in dependent regions

- Peri-hepatic space

- Peri-splenic space

- Pelvis

- Pericardium

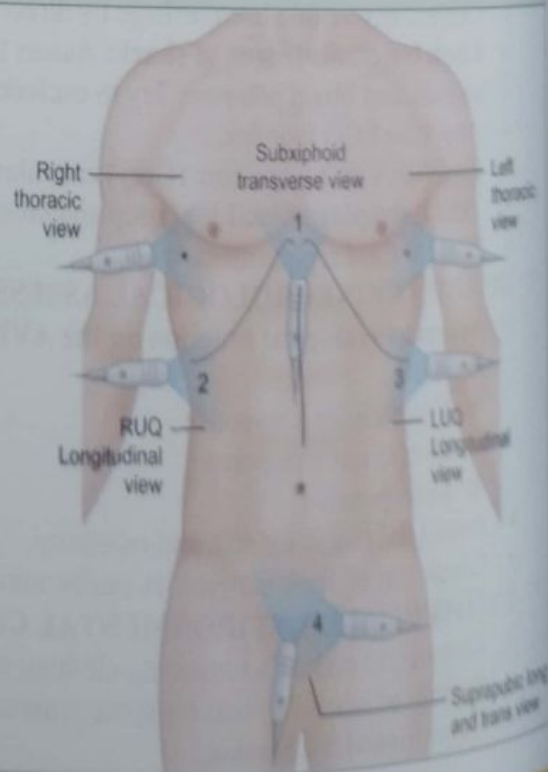
- Pleural fluid/Hemothorax

Pneumothorax:

- Stratosphere sign or barcode sign

FAST

eFAST



APPROACH TO THE MANAGEMENT OF PAIN

International Association for the Study of Pain[®] (IASP) define – Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.

Acute pain: A warning signal indicating actual or potential tissue damage that triggers a protective reaction. Typically associated with trauma, surgery, and acute illness.

Chronic pain: Pain that lasts beyond the normal tissue healing time; (6 months according to the IASP) unlike acute pain, chronic pain has no protective role in preventing further tissue damage and can be considered a disease entity in its own right.

TYPES OF PAIN

- **Noceptive pain:** pain that is triggered by chemical, mechanical, or thermal stimuli (noxious stimuli)
- **Somatic pain (musculoskeletal pain):** localized, sharp pain that varies in duration and quality (A δ fibers)
- **Visceral pain:** dull, diffuse, deep pain (C-fibers).
- **Neuropathic pain:** pain caused by abnormal neural activity that arises secondary to injury, disease, or dysfunction of the nervous system.
- **Central pain:** due to CNS dysfunction from lesions produced by an ischemic stroke, phantom limb pain.
- **Peripheral pain:** due to damage to peripheral nerves (Diabetic neuropathy, postherpetic neuralgia)
- **Sympathetically mediated pain:** due to damage to autonomic nerves (Complex regional pain syndrome)
- **Referred pain:** The pain that is perceived at a location other than that of the causative stimulus; projection of pain usually onto a specific dermatome or myotome of the corresponding segment of the spinal cord.
 - **Referred pain to left shoulder pain** associated with diaphragmatic irritation resulting from haemoperitoneum (**Kehr sign**): Classically secondary to splenic rupture.
 - **Referred epigastric pain to Left chest,** left arm, jaw, neck and shoulder blades: Myocardial infarction.
 - **Referred epigastric tearing pains** to left arm, jaw, neck & shoulder blades: Ruptured aortic aneurysm.
 - **Referred abdominal/epigastric pains** to Groin, Think of: Renal colic/Renal stone.
 - **Referred abdominal pains** to Periumbilical to right iliac fossa, Think of: Appendicitis.
 - **Referred abdominal/epigastric pains** to Back, Think of: Pancreatitis.
 - **Referred abdominal pain** to inferior angle of right scapula blades: Cholecystitis/Gallstone/Cholelithiasis
 - **Referred abdominal pains** to Knee: Hip pain.

Organ involvement	Dermatome involvement	Pain radiation
• Diaphragm	» C4	» Shoulders
• Heart	» T3-4	» Left chest
• Esophagus	» T4-5	» Retrosternal
• Stomach	» T6-9	» Epigastric
• Liver, gallbladder	» T10-L1	» Right upper quadrant
• Small bowel	» T10-L1	» Periumbilical
• Colon	» T11-L1	» Lower abdomen
• Bladder	» T11-L1	» Suprapubic
• Kidneys, testicles	» T10-L1	» Groin

EVALUATION OF PAIN

- For optimal pain management, a complete history & exam is crucial before treatment begins.
- Using the **OD-PARA approach** (or **SOCRATES Approach** as explained in history taking) can help develop your differential diagnosis and to cover all aspects of information.
1. **Onset:** When did the chief complaint occur (gradual, rapid or sudden, intermittent or constant)
 2. **Duration:** When do the symptoms occur? At night, all the time, in the mornings? Etc.
 3. **Progression:** Is this problem getting worse or better? Is there anything that the patient does that makes it better or worse?
 4. **Aggravating factor:** Increase with food or anything?
 5. **Relieving factor:** Relief with food, or with Position change?
 6. **Associated symptoms:** Changes in mobility, strength, and any additional information regarding the chief complaint. Inquire about any other concerns, such as nausea or vomiting.

OD-PARA APPROACH

O- Onset:

D- Duration:

P- Progression:

A- Aggravating factor:

R- Relieving factor

A- Associated features:

آپ کو درد کب سے شروع ہوا؟

آپ کو درد کب تک رہا ہے؟

شروع ہونے کے بعد درد اب تک کب سے چل رہا ہے؟

کمی وجہ سے درد بڑھ جاتا ہو؟

کمی وجہ سے درد کم ہو جاتا ہو؟

درد کے ساتھ آپ نے کوئی اور مسئلہ بھی محسوس کیا ہے؟

درد کے علاوہ کیا آپ نے کوئی اور تکلیف بھی محسوس کیا ہے؟

مریض: کھانسی ہے، بلغم ہے، چھاتی میں درد ہے۔

3) Pain impact (on daily life, sleep, activities)

4) Previous pain assessments and/or treatment

5) Pain intensity scale: subjective grading of pain severity by the patient

» Numeric rating scale (NRS): most common pain scale, evaluates pain on a scale from 0-10.

» Visual analog scale (VAS): visual equivalents suitable for children

» Verbal descriptor scale

6) Take a short, AMPLE history:

» Allergies

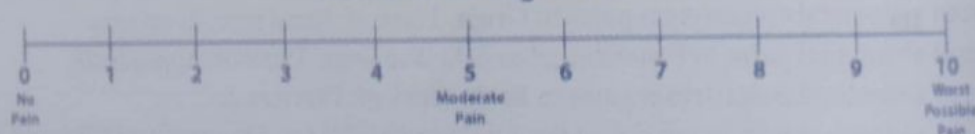
» Medications and tetanus immunity

» Previous/past medical history, Pregnancy

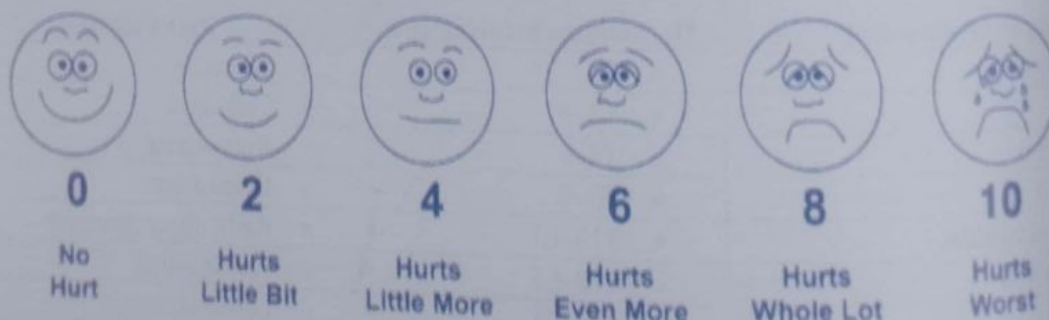
» Last meal

» Events related to injury

Numeric Rating Scale



Wong-Baker FACES® Pain Rating Scale

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PAIN TREATMENT 'WHO ANALGESIC LADDER'

The WHO analgesic ladder is a 3-step algorithm for the management of acute and chronic pain.

1. Regular analgesic (modified-release drugs, administered at fixed times and doses)

» By the mouth: preferably, analgesics should be given orally.

» By the clock: regular administration at fixed times, rather than on demand

» By the ladder (symptom-oriented): if the patient is still in pain, it is necessary to go up a step

2. Appropriate PRN medication (PRN = latin words 'pro re nata' = as needed)

» Short-acting analgesics for peaks in pain

» If PRN medication is required $\geq 3 \times / \text{day}$ → inadequate analgesia likely; review the regular medication

3. Additionally, concurrent treatment with adjuvant drugs

MANAGEMENT OF PAIN USING WHO ANALGESIC LADDER

Step	Pain severity	Nonopioid analgesics	Mild opioids	Strong opioids	Adjuvant drugs
Step-I	Mild	Include	Avoid	Avoid	If required
Step-II	Moderate	Include	Consider	Avoid	If required
Step-III	Severe	Include	Consider	Consider	If required

OPIOID & NON-OPIOID ANALGESICS

Oral non-opioid analgesic		
Drug generic	Drug brand	Drug dose
Paracetamol	» Tab. Panadol 500mg, Tab. Calpol 500mg	TDS/QID
Aspirin	» Tab. Disprin 300mg	TDS/QID
Ibuprofen	» Tab. Brufen 200mg or 400mg or 600mg	TDS
Dexibuprofen	» Tab. Tercica 200mg or 300mg or 400mg	TDS
Flurbiprofen	» Tab. Froben 50mg or 100mg, Cap. Froben 200mg (SR)	BD/ Cap x OD
Mefenamic acid	» Tab. Ponstan forte (500mg), Tab. Mefnac DS (500mg)	TDS
Acetofenac	» Tab. Acenac 100mg or Cap. Acenac 200mg (SR)	BD/ Cap x OD
Diclofenac sodium	» Tab. Voren 25mg or 50mg or 100mg	BD/TDS
Diclofenac potassium	» Tab. Caflam 50mg, Tab. Maxit 50mg or Tab. Maxit 75mg	BD
Naproxen sodium	» Tab. Flaxen 250mg or 500mg, Tab. Proxen 250mg or 500mg » Tab. Synflex 275mg or 550mg, Tab. Aproxen 275mg or 550mg	250mg/275mg = BD/TDS 500mg/550mg = BD
Meloxicam	» Tab. Xobix or Tab. Melfix 7.5mg OR 15mg	BD
Piroxicam	» Tab. Feldene OR Cap. Feldene 10mg or 20mg	BD
Lornoxicam	» Tab. Loxibar 4mg or 8mg Tab. Acabel 4mg or 8mg	BD/OD
Ketorolac	» Tab. Ketor 10mg, Tab. Toradol 10mg, Tab. Kelac 10mg	TDS/QID

Oral opioid analgesic		
Drug generic	Drug brand	Drug dose
Tramadol	» Cap. Tramal 50mg, Cap. Tonoflex 50mg » Tab. Tramal 100mg (SR), Tab. Tonoflex 100mg (SR)	BD/TDS/QID OD/BD/ or TDS
Buprenorphine	» Tab. Bunorfin 0.2mg (200ug), Tab. Mommi 0.2mg (200ug)	BD/TDS
Tapentadol	» Tab. Tapento IR 50mg or 75mg, Tab. Tapoget or Tab. Tanpado	OD/BD/TDS (leaflet)
Morphine	» Cap. Magnus MR 10mg, Cap. Magnus MR 30mg	10 to 30mg x BD/TDS
Methadone	» Tab. Methadone 20mg, Tab. Methadone 40mg	5mg to 20mg x BD/TDS

Oral combine analgesic		
Drug Generic	Drug brand	Drug dose
» Codeine 20mg + Ibuprofen 200mg	» Tab. Brufen Plus	TDS/QID
» Codeine 15mg + Paracetamol 500mg	» Tab. Codogesic	TDS/QID
» Codeine 15mg + Paracetamol 500mg + Caffeine 30mg	» Tab. Napadoc, Tab. Femidol Plus	TDS/QID
» Paracetamol 500mg + Thioridazine 3mg + Caffeine 70mg	» Tab. Diagesic-P	TDS/QID
» Paracetamol 500mg + Ibuprofen 200mg	» Tab. Provas Duo	TDS/QID
» Paracetamol 450mg + Orphenadrine citrate 35mg	» Tab. Neubrol, Tab. Provas-N	TDS/QID
» Paracetamol 650mg + Orphenadrine citrate 50mg	» Tab. Neubrol forte, Tab. Provas-N forte	BD/TDS
» Paracetamol 325mg + Tramadol 37.5mg	» Tab. Tramal Plus, Tab. Tonoflex-P	BD/TDS
» Paracetamol 650mg + Tramadol 75mg	» Tab. Tonoflex-P fort	BD/TDS

Parenteral Non-opioid analgesic		
Drug generic	Drug brand	Drug dose
Paracetamol	» Inj. Provas or Inj. Paracet 1g/100ml x IV infusion	TDS/QID (Max 4g/day)
Ibuprofen	» Inj. Inflame or Inj. Boschofen 400mg/100ml x IV infusion	BD/TDS
Diclofenac sodium	» Inj. Ubrof 800mg/8ml, Inj. Xaleve 400mg/4ml	400mg x TDS/QID
Ketorolac	» Inj. Voren 75mg/3ml, Inj. Dyclo 75mg/3ml x IM	BD
Lornoxicam	» Inj. Toradol 30mg/ml or Inj. Ketor 30mg/ml x IM/IV	BD/TDS
Parenteral opioid analgesic	» Inj. Orno 8mg/2ml or Inj. Acabel 8mg/2ml x IM/IV	OD/BD
Tramadol	» Inj. Tramol 100mg/2ml	TDS/QID

» Nalbuphine	» Inj. Kinz 10mg/1ml, Inj Kinz 20mg/1ml x IM/IV	TDS/QID
» Buprenorphine	» Inj. Buepron 0.3mg/1ml	TDS/QID
» Pentazocine	» Inj. Pentazogon 30mg/1ml	TDS/QID
» Morphine	» Inj. Morphine 15mg/ml	0.1-0.2mg/kg x TDS/QID
» Pethidine	» Inj. Pethidine 100mg/2ml (PDH pharma)	25mg-100mg TDS/QID
» Fentanyl	» Inj. Fentra 50mcg/5ml (0.05mg/5ml), Inj. Fentanyl 100mcg/2ml	Loading dose 25-50 mcg
Analgesic suppositories		
» Paracetamol	» Napa 125mg, 250mg or 500mg suppositories x PR	TDS/QID
» Diclofenac	» Voltral 25mg, 50mg or 100mg suppositories x PR	BD/TDS
Topical analgesics		
» Lidocaine	» Xylocain gel	TDS/QID
» Diclofenac	» Voltral gel, Dicloran gel	TDS/QID
» Ketoprofen	» Dowfen gel, Fastum gel	TDS/QID
» Aceclofenac	» Acenac gel	TDS/QID
» Piroxicam	» Feldene gel, Pcam gel	TDS/QID
Adjuvant analgesics		
1. Anticonvulsants are useful adjuncts in the management of neuropathic pain, commonly used for chronic neuropathic pain.		
» Gabapentin	» Cap. Gaba or Cap. Neogab 100mg or 300mg or 400mg	BD
» Pregablin	» Cap. Syngab 25mg, 50mg, 75mg, 100mg, 150mg	BD/OD
» Carbamazepine	» Tab. Tegral 200mg, Tab. Seizunil 200mg, Tab. Teril 200mg	BD/TDS
» Oxcarbamazepine	» Tab. Oxylapsy 150mg, 300mg, 600mg	BD/TDS
2. Muscle relaxants: Consider muscle relaxants in patients with pain associated with muscle spasticity.		
» Tiznadine	» Tab. Movax or Tab. Musidin 2mg or 4mg	BD
	» Cap. Musidin 6mg, Tab. Fernor SR 6mg	OD
» Cyclobenzaprine	» Tab. Cyclbenz 5mg, Tab. Cyclbenz 10mg	BD
» Eperisone 50mg	» Tab. Myonal 10mg, Tab. Perispa 10mg, Tab. SMUR 10mg	BD/TDS
» Baclofen	» Tab. Lioresal 10mg, Tab. Baclin 10mg	OD/BD
» Thiocolchicoside	» Cap. Muscoril 4mg, Cap. Thiolax 4mg	OD/BD

Non-Opioid analgesic Important considerations

- » Paracetamol is contraindicated in liver failure or active liver disease.
- » The preferred first-line analgesics for mild to moderate pain: Ibuprofen and Naproxen. (Second line is Celecoxib)
- » Selective COX-2 Inhibitor (Celecoxib) Cap. Celbexx 100mg or 200mg is Preferred over NSAIDs in patients with Peptic ulcer disease (PUD) and should be used with caution in patients with renal or cardiovascular disease (CVD).
- » NSAIDs should be used with caution in patients with Peptic ulcer disease (PUD) and patients with kidney disease.
- » NSAIDs is Contraindicated in patients with a recent MI and in the perioperative period of CABG (exception: low-dose aspirin in the management of acute myocardial infarction (acute MI))
- » Avoid NSAIDs in patients with bleeding disorders or those scheduled for surgery/invasive procedures. If possible.

Opioid analgesic Important considerations

- » Combined with nonopioid analgesics (multimodal pain control) to minimize the dose needed for analgesia.
- » Monitor for respiratory depression in the first 72 hours after initiating or increasing the opioid dose.
- » Tramadol is NOT RECOMMENDED in patients with EPILEPSY, as it lowers the seizure threshold.
- » **Contraindications/precautions**
 1. Asthma, respiratory distress, lead to respiratory depression.
 2. Bowel obstruction and maybe not given in Biliary colic as not most opioid are relieving pain.
 3. **Patients with head injury or increased ICP:** Monitor for sedation and respiratory depression. Avoid use of in patients with impaired consciousness or coma susceptible to intracranial effects of CO₂ retention.
 4. Patients with significant respiratory depression
 5. Patients with acute or severe bronchial asthma or hypercarbia in an unmonitored setting or in the absence of resuscitative equipment
 6. Patients with known or suspected paralytic ileus
 7. Patients with hypersensitivity (e.g. anaphylaxis, angioedema)
 8. Patients who are receiving monoamine oxidase inhibitors or who have taken them within the last 14 days due to potential additive effects on norepinephrine levels which may result in adverse cardiovascular events.
- » All patients being discharged with opioid medications should receive counseling on the use of prescription opioids.

FOREIGN BODY ASPIRATION

- Definition: Foreign body aspiration (FBA) is a potentially life-threatening emergency that most commonly occurs in children 1–3 years of age. It is the fifth most common cause of accidental death in children.
- Inhalation of a foreign body into the larynx and respiratory tract, can become lodged in either the upper or lower airway or cause either a partial or complete airway obstruction.
- Symptoms include sudden onset of respiratory distress associated with coughing, gagging, or stridor. Unilateral wheezing suggests partial obstruction of the main or distal bronchi.

Clinical features in foreign body aspiration (FBA)

Complete airway obstruction	Partial airway obstruction	Chronic airway obstruction
- Unresponsiveness. - Inability to breathe or speak. - Ineffective coughing or gagging. - Paradoxical movements of the chest and abdomen - Use of accessory muscles of respiration. - Panic, distress or agitation. - Loss of consciousness (if the obstruction persists). - Absent breath sounds. - Cyanosis	- Choking, persistent coughing or gagging. - Difficulty breathing or shortness of breath. - Hoarseness, wheezing (U/L) or noisy breath - Increased respiratory effort. - Anxiety or distress. - Signs of respiratory distress - Cyanosis, altered mental state - Diminished breath sounds on the affected side Stridor: high-pitched sound when breathing in On inspiration: indicates laryngotracheal localization On expiration: indicates bronchial localization - Hyperresonance on the affected side	- Symptom onset may occur days or weeks later - Persistent or recurrent cough - Purulent or mucopurulent sputum - Wheeze - Fever

MANAGEMENT OF RESPONSIVE PATIENT WITH AIRWAY OBSTRUCTION

- Patient with suspected complete airway obstruction (patient inability to breathe, speak, cry, cough)
 - If the patient **CAN** speak, cry, or cough, **DO NOT TRY Back blows or abdominal thrusts**, as these maneuvers risk dislodging the foreign body and could push the object further and turn a partial obstruction into a complete obstruction.

Protocol for managing airway obstruction in responsive patient:

- Start maneuvers to dislodge the aspirated FB (see table below for technique instructions).
 - Back blows:** preferred initial maneuver in all patients
 - If back blows are ineffective**
 - Infants:** Perform chest thrusts.
 - Adults and children ≥ 1 year old:** Perform abdominal thrusts (Heimlich maneuver).
- Failure to dislodge the foreign body with repeated back blows and chest/abdominal thrusts:
 - If trained:** Proceed with emergency airway procedures for foreign body aspirations.
 - Untrained or instruments not on hand:** Continue maneuvers to remove (dislodge) the aspirated foreign body until help arrives.
- Patient becomes unresponsive.
 - If trained,** proceed to emergency airway procedures in foreign body aspiration (FBA)
 - If not trained,** start CPR (see below "MANAGEMENT UNRESPONSIVE PATIENT").
- NOTE:** If at any time the patient becomes unresponsive despite treatment, start CPR, and, if trained, proceed to emergency airway procedures in foreign body aspiration (FBA).

Maneuvers

Methods for removing/dislodge an aspirated foreign body/foreign object

Infants	Adults and children > 1 year old
1. Initial maneuver: Back blows ☞ Place the infant prone along the provider's forearm with the head lower than the chest. ☞ Support the infant's head by holding the jaw (avoid compressing soft tissues of the neck). ☞ Using the heel of the hand, deliver a back blow between the shoulder blades. ☞ Repeat up to 5 times. ☞ Check if foreign body has removed/dislodged. ☞ If ineffective, proceed to give chest thrusts (see below)	1. Initial maneuver: Back blows ☞ Stand or kneel posterolateral to the patient. ☞ Place one hand on their chest to support their body weight while they lean forward. ☞ Using the heel of the hand, deliver a back blow between the shoulder blades, repeat as needed. ☞ Check if foreign body has removed. ☞ If ineffective, proceed to abdominal thrust (see below)
2. Next step: Chest thrusts ☞ Place the child in a supine position. ☞ Tilt the head back. ☞ Apply pressure swiftly and firmly to the lower third of the sternum (similar location as CPR). ☞ Repeat up to 5 times @ 1 compression per second. ☞ Check if foreign body (FB) has dislodged. ☞ If chest thrusts are ineffective, give another 5 back blows. ☞ Alternate cycles of chest thrusts & back blows as needed.	2. Next step: Abdominal thrusts ☞ Stand or kneel behind the person. ☞ Place one fist slightly above the navel (but below the xiphoid process). ☞ Grasp the fist with the other hand. ☞ Perform a quick inward and upward thrust. ☞ Check if foreign body (FB) has dislodged. ☞ Repeat up to 5 times or until the foreign body (FB) is expelled.

Patient with suspected partial upper airway foreign body aspiration (FBA).

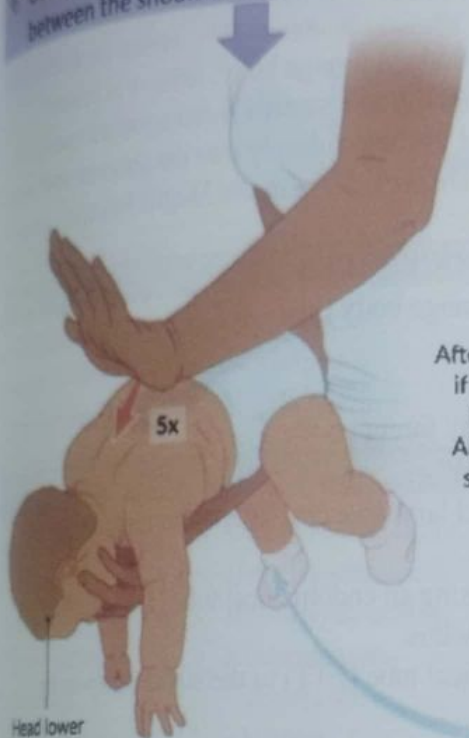
- ☞ Sit the patient upright.
- ☞ Patient should be encouraged to cough to remove the foreign body. If the cough is effective and the foreign body expelled, no external maneuver is necessary.
- ☞ Monitor for signs of deterioration.
 - » Signs of increased work of breathing
 - » Signs of poor gas exchange (e.g., cyanosis)
 - » Weak or ineffective cough
- ☞ **Inability to dislodge the foreign body and patient remains stable:** Immediate Otolaryngology/ENT referral for planned removal of an upper airway foreign body.

Patient with suspected partial lower airway foreign body aspiration (FBA).

- ☞ **Optimize oxygenation:** Check Spo2 → Provide supplemental oxygen therapy to improve oxygenation.
- ☞ Patient should be encouraged to cough to remove the foreign body. If the cough is effective and the foreign body expelled, no external maneuver is necessary.
- ☞ **Inability to dislodge the foreign body and patient remains stable:** Immediate pulmonology referral for planned removal of a lower airway foreign body.

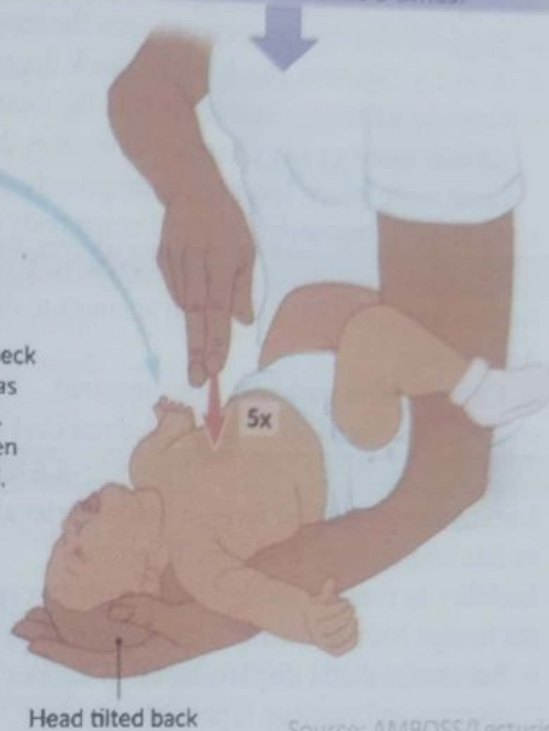
STEP 1

- Back blows between shoulder blades
- Lay baby face down on your forearm
- Using heel of 1 hand, give firm back blows between the shoulder blades.



STEP 2

- Chest thrusts (1/second) to lower third of sternum.
- Lay baby face-up on your forearm.
- Place 2 fingers in the center of baby's chest and compress the breastbone 1.5 inches 5 times.



After each step, check if foreign body has been dislodged. Alternate between steps as needed.

Source: AMBOSS/Lecturio



Heimlich maneuver: (1) The helper stands behind the patient and places their thumb under the xiphoid process, which is located on the upper abdomen. (2) One hand is clenched into a fist. (3) The fist is then grasped with the other hand. (4) Several quick, upward abdominal thrusts are performed with both arms. This causes upward displacement of the diaphragm and, therefore, stimulates coughing. As a result, the foreign body can be mobilized and expectorated from the lower respiratory tract.

Source: AMBOSS

MANAGEMENT OF UN-RESPONSIVE PATIENT WITH AIRWAY OBSTRUCTION CARDIOPULMONARY RESUSCITATION (CPR)

- ☞ Initiate CPR → Chest compressions may dislodge the object by raising intrapulmonary pressure.
- ☞ Attempt to remove the foreign body (FB) while CPR is ongoing.
 - » Head-tilt/chin-lift maneuver to open the airway.
 - » At every 2-minute, check vitals, check the airway for a dislodged foreign body; remove if present.
 - » Consider extracting visible items in the mouth but avoid blind finger sweeps and the routine use of suction-based airway clearance devices as they can impact the object deeply into the pharynx and cause more injury. however, appropriately skilled healthcare providers can use Magill forceps.
 - » Attempt laryngoscopy-guided foreign body (FB) retrieval.

EMERGENCY AIRWAY PROCEDURES

- ☞ Indication: If FIRST AID failed attempts to dislodge the foreign body (FB).
- ☞ Anesthesia:
 - » Unresponsive patients: None required.
 - » Responsive patients: "Scheduled removal of upper airway foreign body."

LARYNGOSCOPY

- ☞ Laryngoscopy-guided foreign body retrieval: Under direct laryngoscopy, attempt to remove any visible foreign body with Magill forceps.
- ☞ Inability to remove foreign body with forceps: Intubate using an endotracheal tube (ETT) to displace the foreign body as distally as possible into either main bronchus.
 - » Successful distal displacement: Withdraw the endotracheal tube (ETT) to the standard tip-to-lip distance and ventilate if possible.
 - » Unsuccessful distal displacement: Emergency surgical airway (see below)

EMERGENCY SURGICAL AIRWAY

- ☞ Indication: failure of the above maneuvers to remove the foreign body in an unresponsive patient
- ☞ Options
 - » Adults: scalpel cricothyroidotomy (or emergency tracheotomy if expertise is readily available)
 - » Infants & children <12 years: needle cricothyroidotomy with percutaneous transtracheal ventilation
- ☞ Further management (after establishing an emergency airway)
 - » Schedules removal of the aspirated foreign body.
 - » Immediately seek advice from relevant department (e.g., ENT, Anesthesia) for a definitive airway.

PROCEDURES FOR PLANNED REMOVAL FOREIGN BODY

1. Planned removal of upper airway foreign body

- ☞ Indication: Stable patients with an upper airway foreign body if attempted maneuvers to dislodge an aspirated foreign body have failed.
- ☞ Anesthetic considerations
 - » Local anesthesia (1% topical lidocaine) can be considered in alert, cooperative patients with an oropharyngeal foreign body (FB)
 - » If general anesthesia is required, IV induction with spontaneous breathing or smooth mask inhaled anesthesia is preferred.
- ☞ Modalities: laryngoscopy (or nasal endoscopy)
- ☞ Procedure: Under direct visualization, the object is grasped and removed with forceps.
- ☞ Risks: Removal of the object can lead to complete airway obstruction; keep equipment on hand to create an emergency surgical airway if needed.

2. Planned removal of lower airway foreign body

Bronchoscopy (gold standard)

- ☞ Indication: stable patient with confirmed suspected lower airway foreign body if Firstaid attempts to dislodge the foreign body have failed
- ☞ Type: flexible bronchoscopy or rigid bronchoscopy (see "Bronchoscopy choice in FBA")
- ☞ Procedure: retrieval of the FB under direct vision
- ☞ Risks
 - » Complete airway obstruction during removal; keep equipment on hand to create an emergency surgical airway if needed.
 - » Pneumothorax
 - » Bleeding
 - » Infection (see "Aspiration pneumonia")
 - » Injury of the tracheal/bronchial wall

EVALUATION & MANAGEMENT OF COMATOSE PATIENT

COMMON CAUSES OF COMA

Structural brain lesions	Metabolic & systemic disorder	Infection and inflammatory pathology	Drug and Toxins Environmental Pathology	Others
Any space occupying lesions/ injury/trauma → can lead to COMA		Any infection or inflammation can lead to COMA	Any drug/poison toxicity, can lead to COMA	
» Traumatic brain injury	» Anoxia & hypoxia (most Common)	» Bacterial, viral or fungal meningitis	» Barbiturate	» Psychogenic coma
» Ischaemic infarction	» Hypercapnia	» Meningoencephalitis	» Organophosphorus	» Hypovolemia
» SDH/EDH/ICH/SAH	» Asthma	» Acute disseminated encephalomyelitis	» Opioids	» Hypoperfusion
» Global cerebral hypoperfusion	» CO ₂ Necrosis	» Severe Sepsis	» Sedative	» Eclampsia
» Hydrocephalus	» Hypotension/shocks	» Syphilis	» Alcohol overdose	» Cardiac causes
» Cerebral venous sinus thrombosis	» Hypo/Hyperglycemia	» Cerebral malaria	» Carbon monoxide	
» Basilar artery occlusion	» Diabetic ketoacidosis	» Waterhouse	» Arsenic poisoning	
» Central pontine hemorrhage	» Hypo/Hyponatremia	» Fredrick's syndrome	» Hypothermia	
» Central pontine myelinolysis	» Hypo/Hypercalcemia	» Complicated typhoid	» Hyperthermia	
» Large hemisphere masses	» Encephalopathy	» Systemic infection	» Heat stroke.	
» Pituitary apoplexy	» Hypertensive		» Snake bites.	
» Cerebral abscess	» Hepatic		» Dog bite	
» Intracranial SOL	» Uremic		» Unknown poison	
» Tentorial herniation	» Metabolic			
	» Wernicke's			
	» Hypoxic			
	» Hepatic/renal failure			
	» Myxedema coma			
	» Adrenal crisis			

GLASGOW COMA SCALE (GCS)

» EYE OPENING	» Spontaneously	4
	» To speech	2
	» To pain	3
	» None	1
» VERBAL RESPONSE	» Oriented (Time, place, and person)	5
	» Confused	4
	» Inappropriate words	3
	» Incomprehensible sounds	2
	» None	1
» MOTOR RESPONSE	» Obeys command.	6
	» Localizes to pain.	5
	» Withdrawals from pain	4
	» Flexion to pain (Decorticate)	3
	» Extension to pain (Decerebrate)	2
	» None	1

Minimum score of GCS: 3

Maximum score of GCS: 15

If GCS is <9, airway should be secured with intubation and protected from aspiration

TREATMENT APPROACH TO THE COMATOSE PATIENT

Rx

A. Airway

- » Ensure patient is maintaining own airway, assess and secure stable airway.
- » Open by Head tilt chin lift / Jaw thrust (**Trauma patient, only Jaw thrust is done:** head tilt, chin lift is never done as it may damage cervical spine)
- » If still closed, use oral or nasal airway.
- » If the airway is still closed, then use advanced airway like; Supraglottic airway device OR endotracheal tube

B. Breathing: Check SpO₂ & Give high flow O₂ as appropriate

C. Circulation:

- » Establish intravenous (IV) access (IV cannula)
- » **Vitals monitoring:** Check BP, PR, RR, Temperature, SpO₂
- » **Obtain laboratory investigation:** after that go with specific investigation according to cause. E.g., Head trauma/Hypertensive encephalopathy → CT brain plain, OPI → S/Cholinesterase level, Hepatic encephalopathy → S/ammonia, Meningitis → CSF D/R & C/S after LP, toxicology screening etc...
- » **IV fluids resuscitation (Ringer's lactate or Normal saline) for correction:** Dehydration, Hypovolemia, Hypotension, Diabetic ketoacidosis (DKA), Hyperosmolar states (HHS) and Hyponatremia
- » **Patient with Hypotension** → by dopamine IV infusion for normal 70kg patient at the rate of 1mcg/kg/min
↳ Inj Dopamine 2 ampule in 100ml 0.9% N/S in IV chamber x 8-drops per minute x SOS
- » **Patient with hypoglycemia:** it is the most important reversible cause of coma. So, Quick bedside RBS, if RBS ≤ 70, immediately give Dextrose 25%/25ml at dose 100ml-150ml x IV to treat hypoglycemia
- » **Patient with opioid toxicity:** Inj Naloxone 0.4mg/1ml x 2AMP x IV stat, 4-6AMP in 1L R/L x IV
- » **COMA COCKTAIL:** when we receive a coma patient from unknown poisoning, initial management after stabilizing ABCD&E is to give coma cocktail IV in which DEXTROSE, THIAMINE (NEUROBION) and NALOXONE 0.4mg/1ml is given.
- » **Patient with seizures:** Inj. Diazepam 10mg/2ml (Valium) x diluted in 8ml 0.9% NS or D5%W at dose 5-10 mg IV as a single dose, may repeat if required. If recurrent treat as status epilepticus (see below)
- » **Patient with Acidosis:** inj. sodium bicarbonate (7.5%) 1 meq/kg, I.V; may be repeated after 10-15 minutes
- » **Empirical IV Antibiotics:** Inj. Ceftriaxone 1-2g are given for suspected meningitis, sepsis, urosepsis, and pneumonia. Culture (Blood, Urine, and CSF) should be done before antibiotics use.
- » **Patient with Hypothermia:** Cover with blankets, continue O₂, correct acidosis by Inj. sodium bicarbonate (7.5%) 1 meq/kg, I.V, to be given over 10 minutes.
- » **Patient with Organophosphorus poisoning:** Inj. Atropine 2-4mg x I.V x stat then as per schedule to be repeated until full recovery OR Start inj. pralidoxime 1-2 gin infusion of 100 ml of normal saline over 30 min
- » **Controlled Reduction of Blood Pressure (For Hypertensive Encephalopathy)**
 - ↳ Inj. Labetalol: 5mg/ml (1 Ampule = 50mg/10ml)
 - **Loading dose:** 10 to 20mg (0.25-0.5 mg/kg; 2-4 mg/min) over 2min x IV x bolus, than give 20mg to 80mg, every 10min until the desire BP goal is achieved. Total dose up to 300mg
 - Use with caution with history of a bronchial asthma, CHF, Chronic bronchitis and emphysema.
 - **IV infusion:** see General drug dilution OR Hypertensive emergency
 - ↳ Inj. Hydralazine 20mg/1ml
 - ↳ 1 Ampule (1ml/20mg) – diluted in 09 ml 0.9% NS, loading dose 10-20mg over 5-10 minutes, than repeat after 20 minutes if desire BP is not achieved.
 - ↳ **IV infusion:** see General drug dilution OR Hypertensive emergency



- » Inj. Sodium nitroprusside: see General drug dilution OR Hypertensive emergency
 - Continuous infusion: 0.3-0.5 microgram/kg/min IV initial infusion, increase in increments of 0.5 microgram/kg/min; titrated to desired effects
 - Rate >2 micrograms/kg/min may lead to cyanide toxicity. Use lowest possible dose. Because prolonged use of sodium nitroprusside carries a risk of cyanide toxicity, it should be limited in dose and duration of use. For infusion ≥ 4 -10 micrograms/kg/min, institute a thiosulphate infusion
- » For profound hyponatremia with seizures (OR) Altered mental status: IV Hypertonic Saline
- » For metastatic CNS lesions with vasogenic edema: IV corticosteroids
- » For Wernicke's encephalopathy: IV Thiamine (Inj. Neurobion)
- » Gastroprotective: Inj. Omeprazole 40mg (Ruling, Risek) OR Inj. Esomeprazole 40mg (Esso, Nexum) x IV x OD
- D. Disability and exposure, along with implementing preventive measures:
 - » Decision to admit the patient is medical HDU/ICU setting/ to hospital ward is based on
 - » Pass nasogastric (NG) tube and Foley's catheterization/ condom catheter with urine bag attachment
 - » Decontamination in case of poisoning (see approach to the patient with poisoning)
 - » Monitor pupillary reflexes (Pupillary size and its response to light)
 - » Record improvement by scoring of Glasgow Coma Scale (GCS)
 - » Brief neurological examination is mandatory to distinguish between true coma and malingering.
 - ↳ Hand drop from the head if patient's tries to control his/her hand, then the patient may be Malingering
 - ↳ Abnormal eye movement Grimacing /withdrawal from noxious Stimulus
 - ↳ Plantar response
 - » Maintain input-output charting. Targeted Urine output should be 0.5ml/kg/hr
 - » Prevention of cutaneous pressure sore (Bed Sore): Frequent change of posture in bed, maintain local hygiene (by alcohol/spirit cleansing); bed should be dry and clean; use air cushions to protect pressure points; apply local antibiotic (with or without povidone iodine and metronidazole ointment) from the beginning of a small bed sore, and consult surgeon.
 - » Care of bladder, bowel and mouth, Constipation should be managed by syp Lactulose 30ml x HS OR Skilex 8-12 drops/2 tab BD/TDS, Mouth care should be done by swabs soaked in boroglycerine/lotion mercurchrome (1%), fungal infection should be tackled by oral Clotrimazole lotion (Clotrim).
 - » Monitor vital signs and regularly including pulse oximetry and continuous ECG monitoring.
 - » Recheck blood glucose and serum electrolytes.
 - » Maintain 'nutrition' and hydration by nasogastric (NG) tube/Ryle's tube feeding (Ensure/Glucerna milk)
 - » Eye Care: Cortosporin/Polyfax eye ointment is applied (prevents exposure keratitis); taping of eyelids, irrigation as and when necessary.
 - » Start physiotherapy as soon as the patient recovers from coma (in CVA cases).
 - » DVT prevention: Move the legs and arms passively thrice daily to prevent leg vein thrombosis and frozen shoulder respectively.
 - » Investigate, identify and treat underlying etiology
 - » In coma, measures to be taken:
 - ↳ Both hypertension and hypotension are deleterious but aggressive control of B.P is not required as it may effect brain perfusion. So, mean arterial pressure (MAP) should be >100 mm Hg
 - ↳ Hypertension: Treated only if MAP is >160 mm hg. Preferred hypotensive agents that do not ↑ ICP by their vasodilating effect like Labetolol or Esmolol should be given
 - » Targeted Urine output should be 0.5ml/kg/hr

TREATMENT OF ACUTE DIARRHEA IN ADULTS

CLINICAL ASSESSEMENT

1. **Clinical History**
 - » **Duration:** Determine the duration of diarrhea (typically less than 2 weeks for acute diarrhea).
 - » **Onset:** Ask about the onset and pattern (sudden or gradual).
 - » **Symptoms:** Assess for associated symptoms such as fever, abdominal pain, nausea, vomiting, or weight loss.
 - » **Recent Travel:** Inquire about recent travel or exposure to **potentially contaminated food or water**.
 - » **Dietary History:** Review recent dietary intake and any potential foodborne illness.
 - » **Medication Use:** Check for recent use of antibiotics or other medications that could impact GI health.
 - » **Exposure:** Ask about exposure to infected individuals or pets.
2. **Physical Examination**
 - » **Assess for signs of dehydration:** dry mucous membranes, decreased skin turgor, reduced urine output.
 - » **Abdominal Exam:** Check for tenderness, bloating, or abnormal bowel sounds.
 - » **Systemic Symptoms:** Evaluate for fever, rash, or other systemic signs that might suggest a specific etiology.
3. **Diagnostic workup**
 - » **Stool analysis:** For signs of blood or mucus, which might indicate inflammatory or infectious causes.
 - » **Stool Culture:** To identify bacterial pathogens (e.g., Salmonella, Shigella, Campylobacter).
 - » **Stool Ova and Parasites:** To check for parasitic infections.
 - » **Stool Antigen Tests:** For specific pathogens such as Giardia or Clostridium difficile.
 - » **CBC:** To assess for signs of infection or inflammation (elevated white blood cell count).
 - » **Urea, Creatinine & Electrolytes:** To evaluate the impact of diarrhea on hydration and electrolyte balance.
 - » **CRP:** To assess for inflammation, particularly in cases of suspected inflammatory bowel disease or infection.
 - » **Abdominal Ultrasound:** If there is concern about structural abnormalities or complications, such as appendicitis or bowel obstruction.

Rx

TREATMENT OF ACUTE DIARRHEA

- » **Oral Rehydration Solutions (ORS):** The primary treatment to prevent dehydration.
 - » **Preparation:** Typically, dissolve 1 packet of ORS in 200-250 mL of clean water.
 - » **Dosage:** Drink 200-400 mL every 1-2 hours, depending on severity and individual needs.
- » **Dietary Adjustments**
 - » **BRAT Diet:** Bananas, Rice, Applesauce, and Toast are recommended initially.
 - » **Avoid:** Dairy products, fatty, spicy, or high-fiber foods until symptoms improve.
- » **Antidiarrheal medications**
 - » **Cap. Loperamide 2mg (Imodium) at dose 4 mg orally** after the first loose stool, then 2 mg after each subsequent loose stool. Maximum dose is 16 mg/day.
 - Note:** Not recommended for diarrhea caused by bacterial infections or in cases of fever or blood in stool (dysenteric diarrhea). Should not be used for > 48 hours without reevaluation of the patient
 - » **Bismuth Subsalicylate (Tab. Bismol 265mg OR Syp. Bismol 88mg/5ml) at dose 30 mL (528 mg) solution PO OR 1,060 mg tablets (=4 tablets) PO every 60 minutes (max. 4,200 mg/24 hours) for up to 2 days**
 - Note:** Avoid if allergic to aspirin or if you have certain medical conditions like kidney disease. Converts to bismuth and salicylic acid in the GI tract. It has antisecretory, antimicrobial, and antiinflammatory effects
 - » **Cap. Racecadotril 100mg (Recada, Hidrasec, Racedo) at dose 100 mg orally, three times daily for 5-7 days.**
 - » Enkephalinase inhibitor that reduces the hypersecretion of electrolytes & water into the intestinal lumen
 - » Appears to be well-tolerated and effective in bacterial diarrhea.
- » **Intravenous fluids:** Indicated for severe dehydration or when oral rehydration is not feasible.
 - » **Typical Solution:** Isotonic solutions such as Normal saline (0.9% NS) or Ringer lactate solution.
 - » **Dosage:** Administer 1-2 liters of crystalloids initially as BOLUS for severe dehydration and reassess the patient's response. The bolus can be repeated based on the clinical assessment and ongoing losses.
 - » **Ongoing Fluid Losses:** Adjust the infusion rate based on the patient's condition, clinical signs of hydration status, and ongoing fluid losses.

ACUTE INFECTIOUS GASTROENTERITIS (FOOD POISONING)

AN OVERVIEW OF COMMON PATHOGENS CAUSING FOOD POISONING (VOMITING &/OR DIARRHEA)

	Foods/transmission	Incubation period
Staphylococcus aureus	Canned meats, mayonnaise/potato salad, custards	1-8 hours
Bacillus cereus	Reheated rice, food kept warm but not hot	Vomiting: 30 min to 6 hr. Diarrhea: 6-15 hours
Clostridium perfringens	Reheated or undercooked meat and raw legumes	6-24 hours
Noroviruses (Norwalk)	Fecal-oral	12-48 hours
Salmonella	Poultry/eggs, meat	Commonly 7-14 days
Enterotoxigenic E. coli (ETEC)	Undercooked meat, endogenous, Fecal-oral	9 hr. to 3 days
Campylobacter jejuni	Poultry, Fecal-oral	2-5 Days
Vibrio	Raw or undercooked shellfish, particularly oysters	Within 24 hours

▲ Food poisoning

C/C:

Foodborne illness, more commonly referred to as food poisoning, is the result of eating contaminated, spoiled, or toxic food.

- » Nausea, vomiting & diarrhea.
- » Abdominal discomfort (pain/spasm/cramps)
- » Epigastric pain
- » Fever maybe present
- » Sign and symptoms of dehydration (mention above)
 - Decrease urination.
 - Dry mouth and throat
 - Feeling thirsty
 - Feeling dizzy, lightheaded
 - Feeling tired & Fatigue

Investigation:

- » Stool analysis &/or Stool culture.
- » CBC: WBCs normal or ↑
- » RFT & electrolytes in dehydration
- » Antidiarrheal: Loperamide (Imodium), Diphenoxylate (Lomotil), may be used in toxigenic gastroenteritis but are contraindicated in invasive gastroenteritis.
- » Probiotics: decrease in the severity and duration of infectious gastroenteritis
- » Empiric antibiotic therapy: Indicated for patients with invasive gastroenteritis, especially if the patient appears ill. Antibiotics are contraindicated in toxigenic gastroenteritis.

Rx

1. Maintain 2 large bore intravenous line.
2. Inj. RL OR 0.9% NS 1L x IV x BD/TDS (calculate acc. to dehydration)
3. Inj. Metronidazole 500mg/100ml (Flagyl, Flazol) x IV x TDS
4. Inj. Omeprazole 40mg (Ruling, Omezol) x IV x OD
5. With Abdominal spasm/pain: Inj Drotaverine 40mg (Nospa, Relispa) x Diluted in 100ml 0.9% N/S x IV x BD/TDS/SOS
6. With vomiting – consider ONE of the following anti-emetics:
 - ⚡ Inj. Metoclopramide 10mg/2ml (Metaclon) x IV x TDS
 - ⚡ OR Inj. Dimenhydrinate 50mg/ml (Gravinate) x IV x TDS
 - ⚡ OR Inj. Ondansetron 8mg/4ml (Onset, Onseron) -Diluted in 50-100ml 0.9% NS over 15 minutes.
7. Inj. Ciprofloxacin 200mg/100ml (Novidate, Ciplet) x IV x BD
 - » Recommendation of Antibiotics: Antibiotics are not given very often for most common types of food poisoning.
 - » If diarrhea is very severe or associated with fever or patient with weak immunity, antibiotics may be considered.

Rx

Discharge patient on the following

1. Tab. Ciprofloxacin 500mg (Ciplet, Novidat, Ciproxen) 1-0-1 (BD) for 3 days
OR Tab. Azithromycin 500mg (Azomax, Zetro) 0-0-1 (OD) for 3 days
2. Tab. Metronidazole 400mg (Flagyl, Klint)
OR Tab. Metronidazole 400mg + Diloxanide 500mg 1-1-1 (TDS) (Flagyl plus, Entamizole DS)

With abdominal pain/spasm

3. Tab. Drotaverine 80mg (Nospa forte, Relispa forte)
OR Tab. Mebeverine 135mg (Colofac, Spasler-p) 1-0-1 (BD)

With nausea or/& Vomiting

4. Tab Domperidone 10mg (Motilium, Domel) 1-1-1 x TDS 30 min before meal
5. Advice patient to intake more fluid or ORS or fresh juices

BACILLARY DYSENTERY (SHIGELLOSIS)

Clinical features	TREATMENT OF BACILLARY DYSENTERY
SYMPTOMS » Duration: 2 – 7 days » Fatigue, malaise, anorexia » Urgency to defecate (tenesmus) » Abdominal cramping/pain » Profuse inflammatory diarrhea » Bloody and mucoid stools » Passage of formed feces that temporarily relieves the pain. » Features of HUS PHYSICAL EXAM » Fever » Increase bowel sounds. » Abdominal tenderness » Signs of dehydration	 1. Consider Hospitalization/early admission. 2. Establish large-bore intravenous (IV) access. 3. Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂ 4. Obtained labs: CBC, BUN, Creatinine, electrolytes, Stool microscopy, and stools culture and sensitivity. 5. Patients with severe dehydration or vomiting: Initially give IV fluid such as isotonic solutions (0.9%NS or RL). ↳ Normal Saline (0.9%NS) 1L & Ringer's Lactate 1L at 2-4 liters or more over the first 24 hours, guided by ongoing assessment of hydration status and electrolyte levels. ↳ Once the patient is stable, switch to oral hydration (ORS). 6. First line antibiotics therapy shortens duration of dysentery. ↳ Inj. Ceftriaxone 1-2g (Oxidil, Rocephin) x diluted in 100ml 0.9% NS x IV every 24 hours for 5 days. ↳ OR Tab. Ciprofloxacin 500mg (Novidate, Cipesta) x BD for 5 days ↳ OR Tab. Azithromycin 500mg (Azomax) x OD for 3 days. 7. Antispasmodics: Avoid, as they can worsen the condition by prolonging the contact of the pathogen with the gut lining. 8. With fever: Inj. Paracetamol 1g/100ml (Provas, Paracet) x IV x TDS 9. Supportive Care: » Hydration: Oral rehydration therapy (ORT) is essential. For severe dehydration, IV fluids may be necessary. » Nutritional Support: Continue feeding with an age-appropriate diet. Avoid foods that can exacerbate symptoms, like dairy products and high-fat foods.
Diagnostic workup	
» CBC: WBCs normal or ↑, ↑ Hct due to volume depletion, leukocytosis. » Stool microscopy: leukocytes, RBCs » Stool culture and sensitivity: +ve » BUN and creatinine: suggest AKI. » Serum electrolytes if dehydrated.	

• Infection control and prevention:

- » Hygiene: Emphasize proper handwashing with soap and water.
- » Sanitation: Ensure safe drinking water, proper sewage disposal, and food safety measures.
- » Isolation: Infected individuals should avoid handling food and close contact with others until fully recovered.

• Follow-up and monitoring

- » Clinical Improvement: Monitor for resolution of symptoms within a few days of starting antibiotics.
- » Rehydration Status: Ensure the patient remains well-hydrated.
- » Complications: Watch for complications such as hemolytic uremic syndrome (HUS), particularly in children.

• When to seek further medical attention

- » Persistent Symptoms: No improvement within 48-72 hours of starting treatment.
- » Severe Symptoms: Persistent high fever, severe abdominal pain, or signs of systemic infection.
- » Dehydration: Signs of severe dehydration despite rehydration efforts.

TYPHOID FEVER (ENTERIC FEVER)

Enteric fever
C/C: see stages in chapter-infectious disease
Low fever then gradually increases

- Headache
- Relative bradycardia
- Nausea/vomiting
- Weakness and fatigue
- Muscle aches
- Loss of appetite
- Abdominal pain
- Rash (Rose spot)
- Diarrhea
- Hepatosplenomegaly

Incubation period: 5–30 days (most commonly 7–14 days)

Treatment duration: 7 days

Diagnostic workup

- **Most accurate test:** Blood culture is the most important diagnostic test at disease onset, as stool cultures are often **-ve** despite active infection.
- **Blood culture**, which is **+ve** in the first week of illness in 80% of patients who have not taken antibiotics.
- **Gold standard:** Bone marrow culture, but rarely performed
- **Complete Blood Count (CBC)**
 - Anemia: ↓ Hb
 - Leukopenia or leukocytosis
 - Absolute eosinopenia
 - Relative lymphocytosis
- LFTs: maybe abnormal
- USG abdomen: Hepatosplenomegaly
- X-ray abdomen: For suspected perforation

IMPORTANT NOTES:

- If free air on x-ray abdomen, Laparotomy should be performed as soon as possible to repair the perforation.
- Specific antibiotics therapy should be started to cover bowel flora.
- Corticosteroid therapy is beneficial in some patients with severe enteric fever and coma, delirium, or shock. Corticosteroids can mask the signs and symptoms of abdominal perforation and should not be continued for more than 48 hours.
- Salicylates (Aspirin) should be avoided.

Rx

- Stabilize patient using ABCD&E approach.
- Establish large-bore intravenous (IV) access.
- Consider early HDU/ICU admission in complicated cases.
- **Vitals monitoring:** Check BP, PR, RR, Temperature, SpO₂
- **Obtained labs:** CBC, BUN/urea, creatinine, electrolytes, LFTs, blood sugar level and blood culture and sensitivity.
- **Hydration:**
 - » **IV Fluids:** Normal saline or Ringer's lactate to correct dehydration and electrolyte imbalances.
 - » **Oral Rehydration Solution (ORS):** Use if the patient can tolerate oral intake.
- **Nutritional Support:**
 - » Provide a high-calorie, easily digestible diet.
 - » Small, frequent meals to avoid gastrointestinal distress.
- **First-line Antibiotics:**
 - » Inj. Ceftriaxone 2g (Oxidil) IV once daily for 10–14 days.
 - » OR Tab. Azithromycin 500mg (Azomax) 1g orally on the first day, followed by 500 mg orally once daily for 7 days.
 - » OR Inj. Azithromycin 500mg (Azitma) diluted in 100ml 0.9% Normal saline x IV x OD
- **Alternative Antibiotics (based on susceptibility testing):**
 - » Tab. Ciprofloxacin (Novidate) at dose 500–750 mg orally twice daily for 7–10 days, though resistance is common.
 - » For multi-drug resistant (MDR) or extensively drug-resistant (XDR) strains: Inj. Meropenem 1g (Meronem) at dose 1 g IV every 8 hours.
- **Gastroprotective:** Inj. Omeprazole 40mg (Risek) x IV x OD
- **Fever:** Inj. Paracetamol 1g/100ml (Provas) x IV x TDS/SOS
- **Corticosteroids:** If indicated, Inj. Dexamethasone 4mg/ml (Decadron) is administered at doses of 3mg/kg initially, followed by 1 mg/kg every 6 hours for 48 hours.
- **With vomiting – consider ONE of the following anti-emetics:**
 - ↳ Inj. Metoclopramide 10mg/2ml (Metaclon) x IV x TDS
 - ↳ OR Inj. Dimenhydrinate 50mg/ml (Gravinate) x IV x TDS
 - ↳ OR Inj. Ondansetron 8mg/4ml (Onset, Onseron) - Diluted in 50–100ml 0.9% NS over 15 minutes.

TREATMENT FOR CARRIER

- **Tab. Ciprofloxacin 750mg** (Hiflox, Quinolox) x BD for 4 weeks has proved to be highly effective in eradicating the carrier state
- Relapses of typhoid fever may be treated with the same antibiotics regimen as the initial attack (see infectious disease)
- When the isolate is susceptible, treatment of carriage with Cap. Ampicillin 500mg (Penbritin), Tab. Co-trimoxazole (Septran DS), Cap Chloramphenicol 250mg (Chloromycetin) may be successful
- Salmonella may sequester in the gallbladder. Cholecystectomy may be required if prolonged antibiotics therapy fails.

SEVERE FALCIPARUM MALARIA

 Severe falciparum malaria
C/C:

General symptoms of malaria

- » Fever with chills, rigors & fatigue
- » Malignant tertian malaria - Irregular fever spikes without a noticeable rhythm
- » Headache and sweating

Malaria organ-specific symptoms

- » **Blood:** thrombocytopenia ($\uparrow$ bleeding risk), hemolytic anemia (weakness, pallor, dizziness)
- » **Gastrointestinal:** Nausea, vomiting, diarrhea, abdominal pain and anorexia
- » **Musculoskeletal:** myalgias, arthralgia
- » **Liver:** Hepato-splenomegaly, jaundice
- » **CNS:** hallucinations, confusion, ALOC, seizures, coma

FEATURES OF SEVERE MALARIA

- » **General:** Prostration
- » **CNS:** Hallucinations, confusion, altered level of consciousness (ALOC), seizures, coma
- » **Cardiac:** Shock (hypotension, capillary refill time ≥ 3 seconds), acute heart failure
- » **Respiratory:** ARDS, pulmonary edema
- » **Renal:** Flank pain, oliguria, hemoglobinuria, acute kidney injury (AKI)
- » **Gastrointestinal:** Jaundice
- » **Hematopoietic:** Significant bleeding

DIAGNOSTIC APPROACH

- » **CBC:** Hb < 7 g/dL (severe anemia)
- » **Serum glucose:** < 40 mg/dL (Hypoglycemia)
- » **ABGs:** Acidosis – base deficit > 8 meq/L or bicarbonate (HCO_3) < 15 meq/L
- » **Serum lactate:** > 5 meq/L (Hyperlactatemia)
- » **Serum BUN/Creatinine:** creatinine > 3 mg/dL or urea > 20 mmol/L
- » **LFTs:** elevated bilirubin, elevated ALT & AST
- » **Coagulation profile:** PT moderately $\uparrow$
- » **Giemsa stained thick & thin blood smears**
 - ↳ **Diagnostic & confirmatory test**
 - Best initial test: Thick blood smear
 - Gold standard test: Thin blood smear
 - ↳ Reveals a high malaria parasitemia – detection of asexual or sexual forms of the parasites inside erythrocytes
 - ↳ **Blood parasitemia** $> 5\%$ OR $> 200,000$ parasites/ μmL .
- » **Malaria RDTs** (Rapid diagnostic tests) OR **MP-ICT:**
 - ↳ Detection of malaria parasite antigen or enzymes
- » **USG abdomen:** Hepatosplenomegaly



SEVERE MALARIA IS A MEDICAL EMERGENCY without appropriate treatment, mortality is 100%

- » Stabilize patient using ABCD&E approach
- » Establish large-bore intravenous (IV) access
- » Pass nasogastric (NG) tube & Foley's catheter with urine bag
- » Consider early HDU/ICU admission
- » **Vitals monitoring:** Check BP, PR, RR, Temperature, SpO₂ (Check SpO₂ & Give high flow O₂ as appropriate)
- » **Monitor pupillary reflexes and record GCS level**
- » **Obtained labs:** CBC, BUN, creatinine, electrolytes, PT APTT & INR, LFTs, CRP, blood glucose and Blood film for malaria parasite
- » **IV fluid:** Dextrose 5% 1L x OD, R/L or 0.9% NS x 1L x IV x BD
- » **Correction of electrolyte and acid-base disturbances**
- » **PARENTERAL ANTIMALARIAL REGIMEN**
 - ↳ **Inj. Artemisinin 30mg/vial, 60mg/vial & 120mg/vial x IV/IM**
 - » Available brand: Gen-M, Hi-sunate, Artisurge
 - » Dosage: 2.4mg/Kg x BD then 2.4mg/Kg x OD for 2 days OR 2.4mg/Kg/dose x STAT, then 12 and 24 hours then 2.4mg/Kg daily for 2 days.
 - » **Reconstitution/Dilution method**
 - **For IV route: STEP 1:** First Add Sodium Bicarbonate Inj. 5% in vial & mix well until clear solution. **STEP 2:** For IV use: Add 2.5ml Sodium Chloride Inj. 0.9% in vial (Step 1) and mix well and use by slow IV route over 2-3 min (Do not put solution in IV drip).
 - **For I.M use:** Add 1ml Sodium Chloride Inj. 0.9% in vial (Step 1) and mix again and use by I.M route.
 - ↳ **ARTESUNATE IS 1ST LINE TREATMENT:** It should be given until the patient is able to take oral treatment (but for at least 24 hours) and parasitemia has fallen to $< 1\%$ (usually a minimum of 3 doses is suggested), followed by a suitable oral anti-malarial regimen.
 - ↳ If parenteral Artesunate is not available – WHO recommended one of the following – a cochrane review found that **ARTEMETHER is more effective than QUININE.**
 - » **Inj. Artemether 80mg/1ml** (Artem, Arceva) at 3.2mg/kg x IM, then 1.6mg/kg/day x IM
 - » OR **Inj. Quinine dihydrochloride 300mg** (Zafquin) at dose 20 mg/kg x IV diluted in 500ml D5%W over 4 hours, then 10 mg/kg IV every 8 hours (TDS)
- » **With fever:** Inj. Paracetamol 1g/100ml (Provas) x IV x TDS/SOS
- » **Consider IV antibiotics cover for secondary bacterial infection:**
 - ↳ **Inj. Ceftriaxone 2g** (Oxidil, Titan, Rocephin) x IV x OD, dilute in 100ml 0.9% NS (or on the basis of culture reports)
- » **IV Gastroprotective:** Inj. Omeprazole 40mg (Ruling, Risek) x IV x OD
- » **Control of seizures:** Follow status epilepticus protocol below.
- » **With vomiting – consider ONE of the following anti-emetics:**
 - ↳ **Inj. Metoclopramide 10mg/2ml** (Metaclon) x IV x TDS
 - ↳ OR **Inj. Ondansetron 8mg/4ml** (Onset, Onseron) x diluted in 50 to 100 ml of 0.9% NS OR D5%W, IV over 15 minutes.
- » **For Acute kidney injury (AKI):** Hemofiltration or hemodialysis (consult and refer to nephrologist)

STATUS EPILEPTICUS

Status epilepticus (SE): It is a life-threatening neurologic condition defined as 5 or more minutes of either continuous seizure activity or repetitive seizures without regaining consciousness. The diagnosis is established after 5 minutes in generalized tonic-clonic seizures and 10 minutes in focal impaired awareness seizures, although long-term neurologic consequences are not likely to occur unless status epilepticus persists for 30 minutes for generalized tonic-clonic seizures or 60 minutes for focal impaired awareness seizures.

3



1. Airway:

- » Ensure patient is maintaining own airway. Assess and secure stable airway
- » Suction of the airway to clear secretion - reduced aspiration
- » Intubate the patient if status epilepticus or trauma

2. Breathing: Check SpO₂ & Give high flow O₂ as appropriate → SpO₂ should be monitored continuously.

3. Circulation:

- » Establish large-bore intravenous (IV) access (to avoid venous irritation and tissue damage due to phenytoin)
- » Send blood test: CBC, urea, creatinine, electrolytes, LFTs, Blood glucose, calcium, magnesium, phosphorus, ABGs and serum anticonvulsant medication levels (in case of convulsive status epilepticus)
- » Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂
- » Patient with hypoglycemia (glucose <60 mg/dL) Dextrose 25%/25ml at dose 50-100ml (2-4 ampule) x IV x STAT

PATIENT WITH ACTIVE SEIZURES/STATUS EPILEPTICUS

➤ First line – Benzodiazepine (Lorazepam, Diazepam, Midazolam)

- » Inj. Diazepam 10mg/2ml (Valium) x diluted in 8ml 0.9% NS x at dose 5-10mg (0.15mg/kg) x IV over 5 minutes as a single dose, may repeat once if necessary (maximum 10mg/dose)
- » OR Inj. Midazolam 5mg/5ml (Dormicum) at dose 10mg x IV, as a single dose, may repeat once after 10 minutes if necessary (Midazolam 10mg x IM is more effective and at least as safe as 4mg of IV)

Reference: Tintinalli's Emergency Medicine 9th edition, Page #1158; CMDT-2023, page #983

➤ Second line – Anti-convulsive agents, If seizures continues:

- » Inj. Phenytoin 250mg/5ml (Epigran) at dose 20mg/kg (maximum 1500mg/dose) in 100ml 0.9% NS x IV over 15 minutes, repeat the dose if not control
- » OR Inj. Sodium valproate 500mg/5ml (Epival) at dose 20-40mg/kg (maximum 3g/dose) x IV over 15min
- » OR Inj. Levetiracetam 500mg (Epilapsa, Lerace) at dose 1-3g (maximum 4500mg/dose) x in 100ml 0.9% NS x IV over 10-15 min

- » If seizures continues: Inj. Phenobarbital 200mg/ml x 20mg/kg x (1-1.5g) x diluted in 100ml N/S x IV

➤ Third line – General anesthesia, If above measures fail

- » Consult specialist for guidance on anesthetic dose
- » General anesthesia with ventilatory assistance may be required: Inj. midazolam 5mg/5ml (Dormicum) may provide control of refractory status epilepticus; the suggested loading dose is 0.2 mg/kg, followed by 0.05-0.2 mg/kg/hour. Inj. Propofol at 1-2 mg/kg/dose as IV BOLUS, followed by infusion at 2-15mg/kg/hr depending on response. Inj. Pentobarbital: may be consider as third line (at dose 5-15 mg/kg x IV, followed by 0.5-4 mg/kg/hour).

4. Disability & Exposure

- » Monitor pupillary reflexes and record GCS level
- » Identify and treat underlying cause, correct electrolytes abnormality
- » Consider IV thiamine^(B1) 100mg (+ B12 200mg & B6 200mcg) – Inj. Neurobion/3ml x IV
- » Radiology: CT scan/MRI Brain (may show hemorrhage, ischemic strokes, edema & tumor, hydrocephalus) & EEG
- » After status epilepticus is controlled, an oral medication program for the long-term management of seizures is started, and investigations into the cause of the disorder are pursued.

DISCHARGE MEDICATION (see epilepsy – section neurology)

1. Tab. Levetiracetam 500mg (Lerace, Epilapsa) x BD (Usual dose/day = 1000mg to 3000mg)
OR Tab. Sodium Valproate 500mg (Epival, Dapakan) x BD/TDS (Usual dose/day = 1500mg to 2000mg)
OR Tab. Carbamazepine 400mg (Tegrol, Seizunil) x BD (Usual dose/day = 400mg to 1600mg)
OR Tab. Brivaracetam 25mg or 50mg (Brivace, Brivatam) x BD (Usual dose/day = 50mg to 200mg)
2. Tab. Clonazepam 0.5mg (Revotril, Naze) x HS

ACUTE HEPATITIS-A VIRUS (HAV) INFECTION

- Hepatitis-A is a viral disease caused by the hepatotropic hepatitis-A virus (HAV). HAV infection can cause acute viral hepatitis, which initially manifests with prodromal symptoms, followed by jaundice.
- Transmission: spreads through fecal-oral transmission
- Incubation period: 2-6 weeks (average 30 days)

Clinical features

Common symptoms

- Initial prodromal phase: 1-2 weeks
 - Fatigue, malaise, arthralgia, myalgia
 - Nausea, vomiting and diarrhea.
 - Poor appetite.
 - Right upper quadrant (RUQ) pain
- Icteric phase: =2 weeks
 - Jaundice
 - Dark urine and pale stools
 - Pruritus

- Physical exam: Jaundice, Scleral icterus, tender liver, tender splenomegaly, right upper quadrant (RUQ) tenderness

Diagnostic workup

INITIAL LABORATORY INVESTIGATION

- CBC: anemia, thrombocytopenia, leukocytosis and leukopenia
- Liver function tests (LFTs):
 - AST & ALT: ↑ (AST/ALT ratio, usually <1)
 - Total bilirubin: ↑
 - Cholestatic markers: ALP ↑ & GGT ↑
- Urinalysis: urine bilirubin ↑, proteinuria

CONFIRMATORY BLOOD TESTING

- Anti-HAV IgM antibodies: ↑ (present in patients with active infection)
 - Usually detectable 5-10 days after exposure and 5-10 days before clinical symptoms develop
 - Levels peak commonly =1 month after infection. May persist for up to 6 months after infection
- Anti-HAV IgG antibodies: ↑
 - Develop during active infection and persist indefinitely after infection or vaccination. Production begins within 2-3 weeks of infection)
- HAV RNA can be detected in stool and serum samples using PCR
- Obtain HBsAg & AntiHCV

Radiological testing: Ultrasound abdomen

Rx

THERE IS NO SPECIFIC TREATMENT FOR ACUTE VIRAL HEPATITIS MANAGEMENT IS CONSERVATIVE – SELF-LIMITING CONDITION.

- Stabilize patient using ABCD&E approach.
- Establish large-bore intravenous (IV) access.
- Consider early admission in complicated cases.
- Vitals monitoring: Check BP, PR, RR, Temperature, SpO2
- Obtained labs: CBC, LFTs, Urinalysis & anti-HAV IgM Ab test.
- IV fluid therapy: Dextrose 5% or 10% x IV x BD
- Inj. L-Ornithine L-Aspartate 5g (Hepamerz) 2-4 Ampule diluted in 300-500ml of Dextrose 5% x slow IV within 4hr
 - Infusion rate: 5g = 1 ampule/hour
 - Maximum 8 ampule per day (8g/day)
 - High doses should be monitored through serum urea, creatinine, and electrolytes.
- With vomiting – consider ONE of the following anti-emetics:
 - Inj. Metoclopramide 10mg/2ml (Metaclon) x IV x TDS
 - OR Inj. Dimenhydrinate 50mg/ml (Gravinate) x IV x TDS
 - OR Inj. Ondansetron 8mg/4ml (Onset, Onseron) x diluted in 50 to 100 ml of 0.9% NS OR D5%W, IV over 15 minutes.
- Counseling, supportive care and discharge medication
 - Use hepatotoxic medication with caution (Paracetamol)
 - Give appropriate nutrition.
 - Advice fresh juices, soft diet, vegetables, fruits
 - Avoid meat, junk food and heavy food.
 - Consider oral glucose intake (GLUCOSE-D SACHETS) 2-3 teaspoonful x 3-4 times a day in a glass water.
 - Syp. Jetepar or Syp. Hepamerz x 1-2 TSP x TDS
 - Tab. Silymarin 200mg (Silliver) x BD OR Syp Silliver 2 teaspoonful x TDS

N.B. The presence of anti-HAV IgM antibodies or HAV RNA confirms active hepatitis-A. Detection of anti-HAV IgG antibodies in the absence of anti-HAV IgM antibodies indicates immunity against HAV due to prior infection or vaccination.

EPISTAXIS (BLEEDING THROUGH NOSE)

Etiology/Risk factors

Strong risk factors

- **Dry weather and low humidity:** often occurs in cold, it can dry nasal mucosa, resulting in excoriation and cracking.
- **Prior nasal or sinus surgery:** Can increase the risk of bleeding
- **Nose injury/trauma:** Nose picking prevents healing of any existing injury. Overly vigorous rubbing during nose blowing can excoriate mucosa (mainly on septum).
- **Nasal fracture** (laceration and avulsion of intranasal tissues) and **maxillofacial trauma**
- **Topical nasal drugs:** nasal corticosteroid & illicit drugs (cocaine) may result in mucosal irritation and bleeding
- **Nasal oxygen cannulae or CPAP** (particularly if not humidified) can cause drying of the anterior nasal septum
- **Medications:** Aspirin, anticoagulants, anti-platelets, non-steroidal anti-inflammatory drugs (NSAIDs)
- **Primary coagulopathy:** Hemophilias most common, in one third cases of von Willebrand disease (VWB disease), and occurs in 5% of patients with immune thrombocytopenia (ITP).
- **Familial hereditary hemorrhagic telangiectasia and juvenile nasal angiofibroma**
- **Chronic liver and kidney diseases:** Can be associated with bleeding tendency.

Weak risk factors: Septal deviation, nasal foreign body, Environmental irritants (dust, chemicals), barotrauma, sinonasal neoplasm, ulceration secondary infection (Herpetic, HIV, bacterial rhinosinusitis, allergic rhinitis), chronic granulomatous disease (Granulomatosis with polyangiitis and sarcoidosis), Hypertension (does not cause bleeding but prolongs existing bleeding)

APPROACH TO THE DIAGNOSIS OF EPISTAXIS

Clinical diagnosis: Based on patient history (current nosebleed or history of nosebleeds) & physical examination.

HISTORY KEY FACTORS:

• In any case of epistaxis, it is important to know:

1. Mode of onset. Spontaneous or fingernail trauma.
2. Duration and frequency of bleeding.
3. Amount of blood loss.
4. Side of nose from where bleeding is occurring.
5. Whether bleeding is of anterior or posterior type

• **Blood is usually found on both sides nose** by the time a patient presents with active epistaxis.

• **Bleeding starting at the nares:** Suggests an anterior site for the source of bleeding. Anterior epistaxis quickly causes blood in the pharynx, so identifying whether a bleed started in the front or down the throat is helpful. Anterior epistaxis will present in the throat if originating while the patient is supine.

• **Recurrent epistaxis:** Self-limited, recurrent significant nosebleed suggests anterior vessel on affected side.

• **Septal deviation:** May increase likelihood for epistaxis. Should be noted because it may impair placement of packing, or mucosal damage may occur due to abrasion while packing is placed.

• **Tachycardia:** may be due to hypovolemia, anemia, anxiety, or pain (from packing placement or cautery).

• **Less common history key factors:** weakness, dizziness, light-headedness, pallor, fainting/syncope, hypotension, bleeding starting in the throat, hypoaesthesia and pain

Diagnostic workup

- **Complete blood count (CBC):** Hb and hematocrit usually normal; low if prolonged or large amount of bleeding
- **Coagulation profile (PT, aPTT & INR, Platelets count):** usually normal; abnormal if coagulopathy
- **BUN/serum urea, serum creatinine:** usually normal; abnormal if liver disease, renal disease, volume depletion
- **Liver function tests (LFTs):** usually normal; abnormal if underlying liver disease
- **Antineutrophil cytoplasmic antibodies (ANCA):** usually normal; abnormal in granulomatosis with polyangiitis
- **serum ACE:** usually normal; abnormal in the presence of sarcoidosis
- **CT scan of paranasal sinuses:** usually normal; may demonstrate: fracture; expansile, erosive process suggesting neoplasm; sinus opacification if sinusitis or neoplasm; intranasal soft-tissue density if polyposis present
- **MRI brain:** normal; may show neoplasm; sinus opacification if sinusitis; intranasal soft-tissue density; fracture
- **Internal and external carotid angiography:** For refractory and complicated epistaxis despite otolaryngology involvement. vascular structure to the nose displayed, may identify vascular anomaly
- **Nasal endoscopy and nasopharyngoscopy:** very useful diagnostic test, may reveals bleeding site and neoplasm
- **Plain nasal & sinus x-ray:** normal or may reveal fracture, or expansion or erosion of structures due to neoplasm

TREATMENT APPROACH OF EPISTAXIS

EPISTAXIS IS THE COMMONEST ENT EMERGENCY



- ☛ Stabilize patients using ABCD&E approach.
 - ☛ Stop causative medications.
 - ☛ Establish large-bore intravenous (IV) access.
 - ☛ Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂
 - ☛ Obtained important labs if indicated: CBC, BUN, electrolytes, creatinine, LFTs, blood glucose, coagulation profile.
 - ☛ Immediate hemodynamic support if patient present with hemorrhagic shock (IV fluid, vasopressors, inotropes)
 - ☛ IV fluid therapy: Ringer lactate, Normal saline x BD/TDS
 - ☛ Keep the patient's head elevated and tilted forward.
 - ☛ Control bleeding by applying uninterrupted, bilateral pressure.
 - ☞ Clear the nose of blood clots: First, ask the patient to blow the nose to expel clots to prepare mucosa for topical vasoconstrictors. Instill a topical vasoconstrictor such as oxymetazoline or phenylephrine.
 - ☞ Pinch the nasal ala against the nasal septum: The patient should lean forward in the "sniffing" position and pinch the soft nares between the thumb and the middle finger for a full 10 to 15 minutes and breathe through the mouth.
 - ☛ Perform anterior rhinoscopy to identify the source of bleeding.
 - ☛ Management of ongoing bleeding
 - ☞ For anterior epistaxis with the bleeding site identified, consider:
 - » Topical vasoconstrictors: Oxymetazoline, phenylephrine
 - » Nasal cautery: chemical cauterization with using a silver nitrate stick or electrocautery
 - ☞ If bleeding persists or the bleeding site cannot be identified, place nasal packing.
 - » Perform anterior nasal packing with a nasal tampon, ribbon gauze, or absorbable packing.
 - Discharge if hemostasis is successful.
 - » If unsuccessful, consult ENT and perform posterior packing, with a nasal balloon or Foley catheter.
 - Quite uncomfortable may require opioid analgesic for pain.
 - Admit for monitoring.
 - ☞ For refractory or recurrent bleeding, consider arterial embolization or endoscopic ligation (most common surgical approach) of the nasal bleeding vessel:
 - » Anterior ethmoidal artery for anterior epistaxis
 - » Sphenopalatine artery for posterior epistaxis
 - ☛ Supportive treatment
 - ☞ IV opioid for pain in posterior nasal packing (quite uncomfortable procedure):
 - » Inj. Tramadol 100mg/2ml (Tramol) + Inj. Dimenhydrinate 50mg/ml (Gravinate) dilute in 100ml 0.9% NS
 - OR Inj. Nalbuphine 10mg/ml (Kinz) + Inj. Dimenhydrinate 50mg/ml (Gravinate) dilute in 100ml 0.9% NS
 - ☞ Consider prophylactic antibiotics for patients who require packing.
 - » Inj. Co-Amoxiclavate 1.2g (Augmentin, Calamox) x IV x STAT
 - OR Inj. Ceftriaxone 1 – 2g (Oxidil, Titan) x IV x STAT
 - ☞ Tranexamic acid might be a useful adjunct: Inj. Transamine 500mg-1000mg x IV STAT, then 500mg x BD
 - ☞ Consider anticoagulant reversal after specialist consultation for patients with posterior &/or severe epistaxis.
 - ☞ Investigate, identify and treat the patient for any underlying cause
1. Antibiotics to prevent sinusitis: Duration for 5 – 7 days
 - ☞ Tab. Co-Amoxiclavate 625mg (Augmentin, Calamox) x BD
 - OR Cap Cephalexin 500mg (Ceporex, Keflex) x BD
 - OR Tab. Clarithromycin XL 500mg (Klaricid XL, Claritek XL) x OD
 - OR Tab. Moxifloxacin 400mg (Maxlox, Xefecta) x OD
 2. If recurrent bleed: Cap. Tranexamic acid 500 mg (Transamine) x BD
 3. For analgesia: Tab Paracetamol + Tramadol (Tramal plus, Tonoflex-P) x BD/TDS for 5 days (avoid NSAIDs, Aspirin)
 4. Cap. Esomeprazole 40mg (Esso, Eskem) x OD on empty stomach after breakfast
 5. Tab. Alprazolam 0.5mg (ALP, xanax) x HS, at bedtime
 6. Topical vasoconstrictive medication: Oxymetazoline spray (Vicks sinex) OR Xylometazoline (xynosine, xolisan) x two sprays on each side of the nose every 12 hours for 3 days, can help prevent persistent epistaxis.

HYPOVOLEMIC SHOCK

ETIOLOGY

Hemorrhage causes

- Postpartum hemorrhage & Rupture ectopic pregnancy
- Upper GI bleeding: e.g., variceal bleeding, PUD
- Blunt/penetrating trauma
- Ruptured aneurysm or hematoma
- Arteriovenous fistula
- Exsanguination
- Hemothorax & Hemoperitoneum
- Fracture (femur and pelvis)

Non-hemorrhagic fluid loss

- Gastrointestinal loss: e.g., diarrhea, vomiting
- Increased insensible fluid loss: e.g., burns
- Third space fluid loss: e.g., ascites, bowel obstruction, pancreatitis
- Renal fluid loss: e.g., adrenal insufficiency, drug-induced diuresis.
- Hyperosmolar states: e.g., hyperosmolar hyperglycemic state (HHS)

Classification of hemorrhagic shock

Class	I	II	III	IV
Blood loss (% of total blood volume)	< 15%	15–30%	30–40%	> 40%
Volume loss (in an average adult)	= 750 mL	= 750–1500mL	= 1500–2000mL	> 2000 mL
Heart rate per minute (bpm)	70 – 99	100 – 120	120 – 140	> 140
Systolic blood pressure	Normal	Normal	Decrease	Decrease
Pulse pressure	Normal	Decrease	Decrease	Decrease
Respiratory rate per minute (rpm)	Normal	20 – 30	30 – 40	> 35
Urine output	> 30 mL/hr.	20–30 mL/hr.	5–15 mL/hr.	Absent
Mental status	Normal	Mildly anxious	Anxious, confused	Confused, lethargic

Diagnostic workup

Routine blood testing

- Serum Lactate: ↑ level (> 2 mEq/L) suggests tissue hypoperfusion and is associated with poorer outcomes.
- Arterial blood gases (ABGs)
- Complete blood count (CBC)
 - ↓ Hemoglobin (Hb), ↓ hematocrit (Hct): suggests hemorrhage
 - Leukopenia or leukocytosis: suggests sepsis
- Blood urea nitrogen (BUN) and Serum creatinine: Increase BUN/Creatinine ratio
- Serum electrolytes: Electrolytes abnormalities e.g. Hyponatremia
- Blood glucose level: Hypoglycemia or hyperglycemia
- Liver function tests: maybe deranged
- Coagulation profile: PT, APTT and INR
- Sepsis workup: Urinalysis, blood cultures, urine culture
- Blood typing and cross matching

Radiological testing

- Chest x-ray (CXR)
 - Pneumonia: suggests sepsis
 - Pulmonary edema, cardiac enlargement, or pleural effusions: suggests cardiogenic etiology
 - Pneumothorax or hemothorax: suggests obstructive etiology.
- Ultrasonography (US)
- Echocardiography (ECG): Findings can show evidence of cardiogenic etiology, e.g., arrhythmias, acute coronary syndrome, signs of cardiomyopathy.
- Transthoracic echocardiography (TTE): can more formally assess right and left sided filling pressures and CO
- Abdominal X-ray and CT scan: rule out pancreatitis and bowel obstruction.
- Upper GI endoscopy or EGD (esophagogastroduodenoscopy): esophageal varices & PUD
- Digital rectal exam (DRE): to identify active GI bleeding
- FAST scan: to identify intraabdominal hemorrhage

MANAGEMENT OF HYPOVOLEMIC SHOCK



1. **Airway:** Visually check the airway and Ensure patient is maintaining own airway assess & secure stable airway, consider C Spine (jaw thrust).
 - » Place patient head down to minimize risk of aspiration
 - » Suction maybe requires clearing airway - blood/vomit
 - » Consider elective intubation (ETT) in patient with ALOC or respiratory stat & severe, ongoing hematemesis.
2. **Breathing:** Check SpO₂ & Give high flow O₂ 10-15L/L
3. **Circulation:**
 - » Maintain 2 large bore intravenous (IV) line
 - » Start 1L 0.9% N/S x IV x stat in 20-25 minutes then attach next 1L so that 1500 ml is infused in 1st hour.
 - » **Vitals monitoring:** BP, PR, RR, Temp., SpO₂ x 5-10min
 - » **Assess severity:**
 - ↳ Tachycardia suggests 10% volume loss
 - ↳ Orthostatic hypotension 20% loss
 - ↳ Shock > 30% loss
 - » **Send labs:** CBC (anemia, thrombocytopenia), BUN/urea, creatinine, electrolytes (AKI/ARI), PT APTT & INR, LFTs (Pre-Existing Liver disease), serum lactate and ABGs.
 - » **Blood products:** Transfuse as soon as possible
 - ↳ Consider 'O' Negative blood (universal donor) in emergency
 - ↳ Cross matching with Arrange 2 units/Pint of PCVs
 - ↳ **If massive transfusion is expected:** Consider transfusing packed RBC, FFP, and platelets in a 1:1:1 ratio.
 - » **Fluid of choice is Crystalloid solution:** 0.9% Normal saline or Ringer lactate (Balance fluid) 1L x IV x BD/TDS
 - » **Inotropic agent:** If the patient does not respond to fluid resuscitation, early use of vasopressors should be considered: Inj. Dopamine 2 Ampule in 100 ml 0.9% N/S in IV chamber x 8-drops per min x SOS
 - » Inj. Haemaccel 500ml x IV x stat then SOS
 - » Inj. Vitamin-K x IV x OD/BD/SOS
 - » Inj. Tranexamic acid 500mg/5ml (Transamine, Btrol, Traxacid)
 - Dosage: 500mg to 1g x IV x BD/TDS/or SOS
 - » **Gastroprotective:** Inj. Omeprazole 40mg (Ruling, Risek) x IV x OD
 - » Inj. Ceftriaxone 1g (Titan, Rocephin) x IV x BD (2g x OD)
 - » **If uterine Atony:** start 2nd IV line with crystalloid fluids with 20-30 IU oxytocin at 150ml/hour
4. **Disability & Exposure**
 - » Monitor pupillary reflexes and GCS level
 - » Keep NPO patient
 - » Identify and correct underlying cause as mentioned above
 - » Consider nasogastric tube & folly's catheterization
 - » **Hemostatic control:** should be prioritized
 - ↳ **Begin immediate bedside measures:** e.g., applying pressure, suturing, or stapling open wounds.
 - ↳ **Consult specialist based on underlying etiology and risk stratification:** e.g., surgery, gastroenterology, OB-GYN, interventional radiology.
 - ↳ **Ensure definitive care:** "Management of trauma" "Treatment of upper and lower GI bleeding" "Treatment of abnormal uterine bleeding," "Antepartum hemorrhage" and "Postpartum hemorrhage"



1. Airway:

- » Secure patient's airway
- » Place patient head down to minimize risk of aspiration
- » Suction maybe requires clearing airway - blood/vomitus
- » Consider elective intubation (ETT) in patients with ALOC or respiratory stat and severe, ongoing hematemesis

2. Breathing: Check SpO₂ & Give high flow O₂ 10-15L/L

3. Circulation:

- » Establish 2 Large bore intravenous line x (20 gauge)
- » **Vitals monitoring:** BP, PR, RR, Temperature, SpO₂ x 1-2 hourly
- » **Obtained labs:** CBC (anemia, thrombocytopenia), BUN, creatinine, electrolytes (AKI), PT APTT & INR, LFTs (Pre-existing liver disease)
- » **IV fluid therapy:** start crystalloids fluid (0.9% Normal saline) to maintain blood pressure.
- » **Blood Transfusion:** Based on hemodynamic status and hb levels.
 - ↳ Cross matching with Arrange 2-4 units packed RBCs
 - ↳ Consider FFPs if PT/INR is increased OR active bleeding
- » **Assess severity of bleeding:** Tachycardia suggest 10% volume loss, orthostatic hypotension 20% loss and shock >30% loss
- » **Acid inhibitory drugs:** Inj. Omeprazole 40mg (Ruling, Risek) at dose 80mg IV bolus, followed by 8 mg/hour continuous infusion for 72 hours, diluted in 100ml 0.9% NS. After stabilization and if the patient can tolerate oral medications, switch to 40 mg orally twice daily for 14 days, then 20-40 mg once daily as maintenance.
- » **Continuous IV infusion of octreotide:** Inj. Octreotide 0.1mg/ml (Sandostatin) at dose 100mcg (=0.1mg) x IV bolus followed by 50-100mcg/hour for 2-5 days, diluted in 100ml 0.9% NS. Reduces splanchnic blood flow and portal hypertension and is effective in the initial control of bleeding related to portal hypertension. It is given promptly to all patients with active upper GI bleeding and evidence of liver disease or portal hypertension until the source of bleeding can be determined by endoscopy. OR Inj. Terlipressin 1mg (Terlip) x 2mg x IV x STAT then Inj. Terlip 1mg x IV x four times a day (QID). Terlipressin may be preferred to octreotide for the treatment of bleeding related to portal hypertension because of its sustained reduction of portal and variceal pressures and its proven reduction in mortality
- » **Prophylactic Antibiotics:** Inj. Ceftriaxone 2g (Oxidil) x IV x OD, diluted in 100ml 0.9% NS, for cirrhotic patients with variceal bleeding, prophylactic antibiotics reduce infection risk.

4. Disability & Exposure

- » Keep NPO patient
- » Pass Nasogastric tube and attach bag - monitor x hourly
- » **Bowel care:** Lactulose 20-30ml x BD OR skilex 10-20 drops x BD
- » Identify and treat underlying cause
- » **Radiology:** US abdomen, chest x-ray (CXR), CT abdomen with contrast, CT Angiography

Initial Evaluation:

History Taking: Assess symptoms (hematemesis, melena), previous disorders, medications (NSAIDs, anticoagulants), and alcohol use.

Physical Examination: Check for signs of hemodynamic instability (hypotension, tachycardia), anemia (pallor), or liver disease (jaundice, ascites).

Esophagogastroduodenoscopy (EGD): The gold standard for diagnosing and treating upper GI bleeding. It allows direct visualization, biopsy, and therapeutic interventions.

Imaging:

- » **CT Angiography:** Useful if endoscopy is inconclusive or not feasible.
- » **Radionuclide Scanning:** Used in specific cases to localize bleeding.

Other Diagnostic Tools:

- » **Nasogastric Lavage:** Can help confirm upper GI bleeding and clear the stomach for better endoscopic visualization.
- » **Capsule Endoscopy:** May be used when bleeding source is not identified by EGD

Scoring system for upper GI Bleed

- 1. ROCKALL SCORE
- 2. MODIFIED FORREST
- 3. G-BLATCHFORD SCORE

Initial treatment option

- EGD: Inj. Epinephrine therapy, sclerotherapy, ligation, or thermal coagulation
- Transjugular intrahepatic portosystemic shunt (TIPS)
- Open surgical procedure (splenectomy)

Upper GI Bleed - Hematemesis or melena → EGD → if negative, colonoscopy to rule out lower GI Bleed

HEPATIC ENCEPHALOPATHY

Clinical Assessment and Diagnosis

Clinical Evaluation:

- » **History:** Document liver disease history, recent medications, gastrointestinal bleeding, infections, alcohol use, and dietary habits.
- » **Physical Examination:** Assess for signs of hepatic encephalopathy (altered mental status, asterix, hyperreflexia) and signs of chronic liver disease (jaundice, ascites, splenomegaly).

Laboratory Tests:

- » **Blood Tests:** LFTs, serum ammonia levels, electrolytes, renal function tests, complete blood count (CBC), coagulation profile.
- » **Imaging:** Ultrasound abdomen or CT scan of the abdomen to assess for structural liver changes or other complications.

Rx

TREATMENT OF HEPATIC ENCEPHALOPATHY

1. Establish intravenous (IV) access.
2. **Vitals monitoring:** Check BP, PR, RR, Temperature, SpO₂
3. **Obtained labs:** CBC, Urea, Creatinine, Electrolytes, LFTs, RBS, PT & INR, Urine D/R, Alpha feto-protein level, Total protein AG ratio, Blood ammonia and ABGs.
4. **Specific treatment for Hepatic Encephalopathy**
 - » **Firstline = Lactulose:** Syp. Lactulose (Duphalac, Lilac) x Start with 20-30 mL orally or NG every 2-4 hours until at least 2-3 soft bowel movements per day are achieved, then adjust to maintain 2-3 bowel movements daily. It reduces ammonia production and absorption in the gut.
 - » **Tab. Rifaximin 550mg** (Rifixa, Nimixa) x per orally or via NG twice daily. (Rifaximin – Add to lactulose for recurrent hepatic encephalopathy or if patients do not respond adequately to lactulose alone).
Alternative: Metronidazole may be used if rifaximin is not available.
 - » **Inj. Metronidazole 500mg/100ml** (Flagyl, Klint) x IV x TDS
 - » **Restriction of protein diet:** Initially limit dietary protein intake during acute episodes but ensure adequate nutrition. Gradually reintroduce protein as the patient improves.
- » **Secondary bacterial infection:** Inj. Ceftriaxone 2g (Oxidil) dilute in 100ml 0.9% NS x IV x OD
- » **Gastroprotective:** Inj. Omeprazole 40mg (Ruling, Risek) x IV x diluted in 100ml 0.9% NS x OD
- » **Inj. Dextrose 10%** at the rate of 100ml/hr x IV x OD/BD
- » **Low albumin:** Inj. Albumin 20%/50ml x IV x OD. Helps maintain oncotic pressure, manage ascites, and reduce complications from low albumin levels in liver disease patients.
- » **Identify and correct precipitating factors**
 - » **Infections:** Treat underlying infections with appropriate antibiotics.
 - » **Gastrointestinal Bleeding:** Manage with blood transfusions, endoscopic interventions, & vasoactive drugs.
 - » **Electrolyte Imbalance:** Correct hyponatremia, hypokalemia, or other abnormalities.
 - » **Dehydration:** Rehydrate with appropriate fluids.
 - » **Constipation:** Address with laxatives or enemas.

GRADES OF HEPATIC ENCEPHALOPATHY

STAGES	FEATURES
Stage-1	Anxiety, Mild Confusion, slurred speech, reversed sleep, apathy, asterix
Stage-2	+ Moderate confusion, disorientation, rigidity.
Stage-3	+ Severe confusion, somnolence, incontinent, babinski's sign
Stage-4	+ Coma

ACUTE HAEMOLYTIC TRANSFUSION REACTION

Clinical features:

- Rapid onset during transfusion
- Fever, chills, nausea, flushing
- Pruritus, urticaria
- Back pain, Dyspnea
- Burning pain at the IV site
- Patients in a coma or under general anaesthesia may present with oozing from wounds or puncture sites.
- Sequelae: Renal failure, DIC, Jaundice

Physical exam

- Flushing
- Wheezing
- Hypotension

Obtained Labs: CBC, Urea, Creatinine, Electrolytes, LFTs, RBS, Urine D/R, ABGs.

Confirm diagnosis: Direct Coombs test, plasma free hemoglobin > 25 mg/dL.

Cardiac monitoring and hemodialysis if hyperkalemia secondary to severe hemolysis occurs

Rx

1. Maintain ABCD&E
2. Stop the transfusion immediately.
3. Check the right pack has been given to the right patient
4. Repeat typing and cross-matching of the transfusion product to identify and record causative blood products
5. Establish IV access (Do not flush existing line & use a new IV line if required)
6. Immediate infusion of saline to aid diuresis and manage hypotension
7. **Start Normal Saline (N/S)** x IV x Stat using a new drip set
8. **Hypotension:** Inj. Haemaccel 500ml x IV x STAT then SOS
 - » Inj Adrenalin (Epinephrine) 0.5mg (1:1,000) x IM and repeat every 5 minutes if shock persists
 - » Dose: 0.1mg/ml x IV x STAT than every 5-10 minutes
9. **Obtained labs:** CBC, urea, creatinine, electrolytes, LFTs, RBS, Urine D/R
10. Administer FFP and platelets if DIC develops
11. Give Inj. Pheniramine maleate 25mg/2ml (Avil) x 2ml IV x STAT
12. Give Inj. hydrocortisone 100-250mg (Solu cortif) x 2ml IV x STAT
13. **Fever:** Inj. Paracetamol infusion 1g (Provas) x IV x SOS/TDS

AMOEBIC LIVER ABSCESS

Amoebic Liver Abscess

C/C:

- Fever (either continuous or spiking) with Chills
- RUQ Abdominal pain
- Hepatic tenderness
- Anorexia & weight loss
- Malaise
- Jaundice
- Hepatomegaly

Clinical improvement is often seen within 72 to 96 hours, but treatment should be continued for 7 to 10 days.

Diagnostic workup

- CBC: Leukocytosis, no eosinophilia, mild anemia
- ↑ alkaline phosphatase
- Elevated ESR
- LFTs: AST, ALT, bilirubin are slightly ↑
- Ultrasound Abdomen
- CT scan/MRI abdomen
- Single abscess (80%), usually right lobe, wall enhancement seen on CT scan with IV contrast
- **Positive serology:** Anti-amoebic antibodies

Rx

1. Establish intravenous (IV) access.
2. Vitals Monitoring and RBS x BD/TDS
3. **Start IV fluid:** Dextrose 5% or 10% x 1L @ 10 drops/min x IV
4. Inj. Ketorolac 30mg/ml (Toradol) dilute in 4-8ml water x IV x BD/TDS
5. Inj. Omeprazole 40mg (Risek) diluted in 100ml 0.9% NS x IV x OD
6. **Antibiotics:** Inj. Metronidazole 500mg/100ml (Flagyl) x IV x TDS
PLUS, Inj. Ceftriaxone 2g (Titan, Rocephin) x IV x OD
OR Inj. Ciprofloxacin 200mg/100ml (Novidate) x BD
7. **With vomiting – consider ONE of the following anti-emetics:**
 - ↳ Inj. Metoclopramide 10mg/2ml (Metaclo) x IV x TDS
 - ↳ OR Inj. Dimenhydrinate 50mg/ml (Gravinate) x IV x TDS
 - ↳ OR Inj. Ondansetron 8mg/4ml (Onset, Onseron) x diluted in 50 to 100 ml of 0.9% NS OR D5%W, IV over 15 minutes.
8. Consider Inj Vitamin-K or Konakoin 1ml x IV x OD (3-days)
9. **Invasive procedures**
 - » **Aspiration:** ultrasound or CT-guided puncture of complicated liver abscesses at risk for perforation
 - » **Indications:** Localized in the left lobe, Pyogenic abscess, Multiple abscesses, Failure to respond to pharmacotherapy
10. **Surgical drainage:** should generally be avoided, but may be indicated for inaccessible abscesses or ruptured abscesses in combination with peritonitis. **NOTE:** Drainage is not necessary, even for large abscesses of 5 to 10 cm, except in patients who do not respond within 5 days. The abscess usually will shrink by about 50% within a week, but the mean time to complete radiologic resolution is 3 to 9 months. The overall mortality rate from amebic abscess is 1 to 3%, whereas it is less than 1% if diagnosed and treated early.

PYOGENIC LIVER ABSCESS

Clinical features	<i>Rx</i>
Classic triad of pyogenic liver abscess » Fever (with/without chills & rigors) » Malaise » Right upper quadrant pain Other symptoms » Anorexia and weight loss » Nausea and vomiting » Symptoms of diaphragmatic irritation, Pleuritic chest pain Physical examination » Jaundice » Tender hepatomegaly » Intercostal tenderness » Epigastric tenderness » Decreased breath sounds in right lower lobe of the lung » Features of sepsis	1. Establish intravenous (IV) access. 2. Vitals Monitoring and RBS x BD/TDS 3. Start IV fluid: Dextrose 5% Or 10% x 1L @10drops/min x IV 4. Empiric antibiotic therapy for Pyogenic Liver Abscess » Combination therapy regimens Inj. Metronidazole 500mg/100ml (Flagyl, Klint) x IV x TDS PLUS, any one of the following: ↳ Inj. Ceftriaxone 2g (Oxidil, Titan) x OD OR Inj. Ciprofloxacin 400mg/100ml (Novidate) x IV x BD » OR Single-agent regimens (any of the following) Inj. Piperacillin + Tazobactam (Tanzo 4.5g) x IV x TDS OR Inj. Cefoperazone + Sulbactam 2g (2SUM) x IV x BD OR Inj. Imipenem/Cilastatin 500mg (Cilapen, Tienam) x IV x TDS OR Inj. Meropenem 1g (Meronem, Penro) x IV x TDS Duration: Continue IV antibiotics for ≥ 2 weeks before switching to oral antibiotics. (≥ 2 weeks x IV, than 3-4 weeks PO) Total duration of therapy: typically, 4-6 weeks
Diagnostic workup	
» CBC: Leukocytosis, anemia » LFTs: ↑ alkaline phosphatase and ↑ AST, ALT & bilirubin level » Serum albumin: Low albumin » PT, APTT & INR: Increased INR » Increased ESR, CRP & LDH » Blood culture +ve (upto 60%) » U/S Abdomen (duplex scan) » CT/MRI abdomen: multifocal (50%), usually right lobe, irregular margins » Percutaneous aspiration with Gram stain and culture	5. Pain: Inj. Ketorolac 30mg/ml (Toradol) dilute in 4-8ml NS x IV x TDS 6. Inj. Omeprazole 40mg (Risek) dilute in 100ml 0.9% N/S x IV x OD 7. With vomiting – consider ONE of the following anti-emetics: ↳ Inj. Metoclopramide 10mg/2ml (Metaclon) x IV x TDS ↳ OR Inj. Dimenhydrinate 50mg/ml (Gravinate) x IV x TDS ↳ OR Inj. Ondansetron 8mg/4ml (Onset, Onseron) x diluted in 50 to 100 ml of 0.9% NS OR D5%W, IV over 15 minutes. 8. Consider Inj. Vitamin-K or Konakoin 1ml x IV x OD (3-days) 9. Percutaneous aspiration and culture of the aspirate » Both diagnostic and therapeutic » Performed under US or CT guidance » Aspirated material is cultured to determine the organism and its antibiotic-susceptibility profile

DRAINAGE OF THE ABSCESS CAVITY

- Indicated in nearly all cases of pyogenic liver abscess
- Indication for percutaneous drainage/needle aspiration: solitary abscess
 - Small (< 5 cm) abscess: percutaneous needle aspiration
 - Large (> 5 cm) abscess: percutaneous drainage and intracavitary catheter placement
 - If percutaneous drainage/aspiration fails, a second attempt at percutaneous drainage/aspiration can be made before abscess will require surgical drainage.
- Indications for surgical drainage (open/laparoscopic)
 - Multiple or loculated abscesses
 - Deep-seated abscess not amenable to percutaneous drainage
 - Ruptured abscess
 - Thick viscous pus which cannot be drained percutaneously
 - Underlying disease which requires surgical intervention (e.g., choledocholithiasis, appendicitis)
- Contraindications: coagulopathy (e.g., INR > 1.5; thrombocytopenia due to sepsis)

DENGUE FEVER (WITH SEVERE/PROGRESSIVE THROMBOCYTOPENIA)**Classic dengue fever**

Starts with fever with chills and malaise that lasts ~ 1 week
Severe arthralgia and myalgia (often referred to as "break-bone fever")
Severe headache and retro-orbital pain
Maculopapular, measles-like exanthem (typically appears 2–5 days following fever)
Generalized lymphadenopathy

Dengue hemorrhagic fever (DHF)

Occurs in 1–2% of cases

Current or recent fever lasting 2–7 days →
Generally develops as the initial fever subsides (1 week after onset)

Clinical manifestations

Temperature change: ranges from hypothermia to a second spike in fever,
Abdominal pain, vomiting

Mental status changes (confusion)

Hemorrhagic features: petechiae, epistaxis, gingival bleeding

Positive capillary fragility test

Increased vascular permeability → signs of pleural effusion &/or ascites.

Dengue shock syndrome (DSS): DHF + shock

WARNING SIGN**Clinical**

- » Abdominal pain or tenderness
- » Persistent vomiting
- » Clinical fluid accumulation
- » Mucosal bleed
- » Lethargy, restlessness
- » Liver enlargement >2 cm

Laboratory: Increase in HCT concurrent with rapid decrease in platelet count

Rx

- ☞ Stabilize patients using ABCD&E approach.
- ☞ Establish large-bore intravenous (IV) access.
- ☞ Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂.
- ☞ Obtained labs: CBC (Thrombocytopenia 'platelets <100,000/mm³'), BUN/urea, creatine, electrolytes (AKI/ARI), PT INR, LFTs, MP ICT, Dengue NS1 Ag & Dengue IgM + IgG serology, in severe cases L.P
- ☞ Needs monitoring with CBC: haematocrit (before and after fluid replacement, then 6–12 hourly) and daily platelet count.
- ☞ Give isotonic fluid: Inj R/L or 0.9% N/S 1000ml x IV x OD
 - ☞ Start with 5–7 ml/kg/hour for 1–2 hours, then reduce to 3–5 ml/kg/hr for 2–4 hours, and then reduce to 2–3 ml/kg/hr or less according to the clinical response, Intravenous fluids are usually needed for only 24–48 hours.
- ☞ Platelets transfusion: if platelets count is ≤10,000 or there is any evidence of bleeding from any site with thrombocytopenia.
- ☞ For Fever/analgesia: Inj Paracetamol 1g/100ml (Provas, Paracet) x IV infusion x TDS OR Tab. Paracetamol 500mg (Panadol, Calpol) x PO x 500mg-1000mg (1-2 tablets) x TDS/QID. (Maximum 4g per day)
- ☞ Gastroprotective: Inj. Omeprazole 40mg (Risek, Ruling) x IV x OD.
- ☞ With vomiting – consider ONE of the following anti-emetics:
 - ☞ Inj. Metoclopramide 10mg/2ml (Metaclon) x IV x TDS
 - ☞ OR Inj. Dimenhydrinate 50mg/ml (Gravinate) x IV x TDS
 - ☞ OR Inj. Ondansetron 8mg/4ml (Onset, Onseron) x diluted in 50 to 100 ml of 0.9% NS OR D5%W, IV over 15 minutes.
- ☞ Inj. Neurobion 2ml x put 2 ampules in R/L x OD
- ☞ Tab. Folic acid 5mg x PO x OD/BD
- ☞ Access to ICU to monitor organ failure.
- ☞ Urine output monitoring: about 0.5 ml/kg/hr. x 4-6 hourly
- ☞ Send Urinalysis to check for RBC.

SPECIAL PRECAUTION AND PREVENTION

- ☞ No vaccine can protect against dengue fever. Only avoiding mosquito bites can prevent it. Avoid visiting areas prone to mosquitoes.
- ☞ Avoid exposure, use of mosquito repellent
- ☞ IV crystalloids and colloids given rapidly in severe disease.
- ☞ Encourage adequate hydration, fresh juices, soft diet etc..
- ☞ Avoid Intra-muscular (IM) injection
- ☞ Avoid tooth brushing, shaving and combing as risk of bleeding
- ☞ Avoid antiplatelets (aspirin/clopidogrel), anticoagulants (Heparin/warfarin), NSAIDs and corticosteroids

IRON DEFICIENCY ANEMIA (IDA)

DIAGNOSTIC WORKUP

- ☞ CBC: $\downarrow$ hb (<11 g/dL), $\downarrow$ MCV (<76 femtoliters), $\downarrow$ MCH (Hypochromic) & $\downarrow$ MCHC
- ☞ Peripheral blood smear: Shows microcytic (small) and hypochromic (pale) red blood cells, anisocytosis
- ☞ Serum iron profile (Iron studies)
 - » Reduced: Serum iron, Ferritin, Transferrin saturation ($<20\%$)
 - » Increased: TIBC, TFR and Red Cell Protoporphyrin

TREATMENT OF IRON DEFICIENCY ANEMIA (IDA)

Rx

- ☞ Obtained labs: CBC, iron studies, peripheral blood smears
- ☞ If hypotension: 0.9% NS 1L $\pm$ Inj. Haemaccel x IV x STAT
- ☞ If hemoglobin (Hb) level <7 : Cross matching with Arrange 2 units/Pint of PCVs
- ☞ Intravenous (IV) iron supplements:
 - » Inj. Iron sucrose 100mg (Venofer, Besleri-S) at dose 200mg (2 ampule), diluted in 100ml 0.9% NS regularly for 3 days OR on alternative days (total 3 doses)
 - » OR Inj. Ferric carboxymaltose 500mg/10ml (Fercari, FCM, Elen-Jec), dilute in 100ml 0.9% Normal saline (NS) infuse quickly (using a volumetric infusion pump) over 15 minutes. After infusion flush IV line with 50 mL NS
- ☞ Dosage: Patients weighing 50 kg or more: Two doses of 750 mg each, 7 days apart.
Patients weighing less than 50 kg: Two doses of 15 mg/kg (up to 750 mg per dose), 7 days apart.
- ☞ Adjunct: Inj. Vitamin B1 + B2 + B6 (Neurobion, Neuro-Bedoxine) x IV x STAT on Alternative day x 10 doses
- ☞ Advice dietary modifications
 - » Increase intake of iron-rich foods: red meat, poultry, fish, lentils, beans, leafy green vegetables, fortified cereals, and nuts.
 - » Enhance iron absorption by consuming vitamin C-rich foods (e.g., citrus fruits, tomatoes) alongside iron-rich foods.
- ☞ Identify and treat the underlying disease (e.g., antihelminthics for hookworm, OCPs for menorrhagia)
- ☞ Recheck iron levels: Typically, 4-6 weeks after starting treatment to assess response & adjust dosage as needed.

MEGALOBLASTIC ANEMIA (FOLIC ACID & VITAMIN-B12)

DIAGNOSTIC WORKUP

Note: Blood findings in vitamin B12 and/or folic acid deficiency are similar

- ☞ CBC: $\downarrow$ hb (<11 g/dL), $\uparrow$ MCV (>96 femtoliters), $\downarrow$ WBC count (leukopenia), $\downarrow$ Platelets
- ☞ Peripheral blood smear: Pancytopenia, Macrocytic and oval (egg-shaped macro-ovalocytes), Hypersegmented neutrophils (more than five nuclear lobes)-Hallmark feature
- ☞ Test of choice: $\downarrow$ Serum folic acid level = folic acid deficiency & $\downarrow$ Serum vitamin B12 level = vitamin B12 deficiency

Rx

- ☞ Obtained labs: CBC, serum B12, serum folate, peripheral smear
- ☞ Vitamin B12 deficiency
 - » Inj. Cyanocobalamin + B1 + B2 (Neurobion, Neuro-Bedoxine) x IV x OD for 7 days, then every weekly for 4 weeks than every monthly for the 6 months of duration.
 - » OR Inj. Mecobalamin 500 mcg (Methycobal, Neuromet, Cobalamin) x 2 ampule (=1000mcg = 1mg) x IM, in 5 doses at 2-3 days apart (a total of 5 mg), followed by maintenance therapy of 1000 mcg (1mg) every 3 months for rest of the life.
- ☞ Folate deficiency: Tab. Folic acid 5mg x PO x OD daily for 3 weeks cures acute deficiency, while 5 mg once weekly is sufficient for maintenance therapy.
- ☞ Dietary sources
 - » Folic acid: Leafy green vegetables, citrus fruits, beans, and fortified cereals.
 - » Vitamin B-12: Meat, poultry, fish, dairy products, eggs, and fortified cereals. For vegetarians/vegans, B12-fortified foods or supplements are essential.
- ☞ A sensory neuropathy may take 6-12 weeks to correct, long standing neurological damage may not improve.

ACUTE BRONCHIAL ASTHMA

ASSESSMENT OF ACUTE ASTHMA ATTACK

Clinical features	Mild	Moderate	Severe
	SYMPTOMS		
Breathlessness	While walking	While at rest	At rest
Position	Can lie down	Prefers sitting	Hunched over
Ability to speak	Sentences	Phrases	Individual words
Alertness	Maybe agitated	Usually agitated	Agitated
Clinical features	SIGNS		
Respiratory rate	Increased	Increased	Often >30/minute
Wheezing	Moderate, often only end-expiratory	Loud; throughout exhalation	Throughout inhalation and exhalation; can also be absent
Use of accessory muscles	Rarely	Commonly	Usually
Pulse/minute	<100	100-120	>120
Pulsus paradoxus	Absent	Maybe present	Often present
PCO ₂	<42 mm Hg	>42 mm Hg	≥42 mm Hg
SaO ₂	>95%	90-95%	<90%

Clinical features

- Often worse in the early morning and at night
- Wheezing
- Productive cough
- Shortness of breath
- Chest tightness

- Features in severe cases
- Accessory muscle usage
- Paradoxical breathing
- Decreased breath sounds
- Prolonged expiratory phase
- Tachypnea
- Pulsus paradoxus
- Hyperresonance

Clinical examination

- Auscultation (characteristic findings are usually only present during acute attacks)
- Prolonged expiratory phase with wheezing (dry crackles)
- Decreased breath sounds; possibly "silent chest"
- Tachypnea
- Percussion
- Hyperresonant sound
- Inferior displacement and poor movement of the diaphragm

- In severe attacks: ALOC, Cyanosis



TREATMENT OF ACUTE ASTHMA

- Stabilize patients using ABCD&E approach.
- Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂.
- Administer oxygen to maintain SpO₂ ≥ 92% or as clinically indicated.
- Obtained labs: CBC, Spirometry, serum total IgE, allergen specific IgE.
- Nebulized Salbutamol 5mg/ml solution (Ventolin) at dose 2.5mg – 5mg (0.5-1ml), dilute in 2-3ml 0.9% NS, Give via nebulizer every 20 minutes for up to 3 doses.
- Nebulized Ipratropium bromide 0.025%/2ml (Atem, Atrovent) in 2-3ml 0.9% NS, Give via nebulizer every 20 minutes for up to 3 doses.
- Inj. Hydrocortisone (Solu-cortif, Hyzonate) 100mg-250mg x STAT



TREATMENT OF STATUS ASTHMATICUS

- Stabilize patients using ABCD&E approach.
- Establish intravenous (IV) access.
- Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂.
- Administer oxygen to maintain SpO₂ ≥ 92% or as clinically indicated.
- Obtained labs: CBC, Spirometry, serum total IgE, allergen specific IgE.
- Nebulized Salbutamol 5mg/ml solution (Ventolin) at dose 2.5mg – 5mg (0.5-1ml), dilute in 2-3ml 0.9% NS, Give via nebulizer every 20 minutes for up to 3 doses.
- Nebulized Ipratropium bromide 0.025%/2ml (Atem, Atrovent) dilute in 2-3ml 0.9% NS, Give via nebulizer every 20 min for up to 3 doses.
- Give Inj Hydrocortisone (Solu-cortif) at loading dose 250mg IV Bolus, followed by 100 mg IV every 6-8 hours. The dose can be adjusted based on patient response and clinical guidelines.
- Other therapies under specialist guide:
 - Inj. Magnesium sulphate 500mg/ml at dose 1-2g, diluted in 100ml 0.9% normal saline (NS), given IV over 20-30 minutes.
 - Inj. Salbutamol 5mg (Ventolin), diluted in 500ml 0.9% NS
 - Inj. Aminophylline 250-350mg in 20ml 0.9% NS x IV over 20 minutes loading dose followed by 500mg in 500ml 0.9% NS

Acute Exacerbation of Chronic Obstructive Pulmonary Disease (AECOPD)

Clinical features	TREATMENT OF COPD
Cardinal symptoms of AECOPD: » Worsening of dyspnea » Increased frequency and severity of cough » Increased volume and/or purulence of sputum Possible additional symptoms » Wheezing, tachypnea » Fever, chills Signs of severe AECOPD » Respiratory failure, severe hypoxemia » Signs of increased work of breathing (accessory muscle use, tripod position) » Thoracoabdominal asynchrony » Respiratory acidosis » Altered mental status » Central cyanosis	 ☞ Stabilize patients using ABCD&E approach. ☞ Establish large-bore intravenous (IV) access. ☞ Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂. ☞ Give supplementary oxygen, aims to keep saturation 94-98. ☞ Obtained labs: CBC, Spirometry, serum total IgE, allergen specific IgE. ☞ Nebulized Salbutamol 5mg/ml solution (Ventolin) at dose 2.5-5mg (0.5-1ml), diluted in 2-3ml 0.9% NS, via nebulizer every 20 min for up to 3 doses. ☞ Nebulized Ipratropium bromide 0.025%/2ml (Atem, Atrovent) at dose 0.5mg (2ml) in 2-3ml 0.9% NS, Give via nebulizer via nebulizer every 4-6 hours ☞ Give Inj. Hydrocortisone (Solu-cortif) 250mg-500mg x STAT then SOS, when stable consider oral prednisolone 40mg/day for 7-14 days. ☞ Consider antibiotics if indicated: Inj. Azithromycin 500mg (Azitma) diluted in 100ml 0.9% NS x IV x OD OR Inj. Moxifloxacin 400mg (Moxiget) x IV x OD (most exacerbations may be non-infectious or viral, so antibiotics not usually needed unless clear evidence of bacterial infection) ☞ Gastroprotective: Inj. Omeprazole 40mg (Risek, Ruling) x IV x OD. ☞ Physiotherapy should be offered to help with sputum clearance. ☞ Continuous pulse oximetry and ABGS

ACUTE RENAL COLIC (ACUTE RENAL PAIN)

Clinical features	
» Sudden onset of severe unilateral colicky flank pain » Radiates anteriorly to the lower abdomen, groin, labia, testicles, or perineum » Nausea vomiting » Hematuria » Dysuria, frequency, and urgency » Passage of gravel or a stone	 ☞ Stabilize patients using ABCD&E approach. ☞ Establish large-bore intravenous (IV) access. ☞ Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂ ☞ Obtained labs: CBC, BUN, Creatinine, electrolytes, LFTs, CRP/ESR, Blood sugar, calcium, uric acid level, urinalysis, and urine C&S. ☞ IV fluid: Inj. Ringer Lactate OR 0.9% Normal saline 1L x IV x BD ☞ Pain management/analgesia: ☞ Inj. Paracetamol 1g/100ml (Provas, Paracet) x IV x TDS/SOS ☞ OR Inj. Ketorolac 30mg/ml (Toradol) in 4ml 0.9% N/S x IV ☞ OR Inj. Tramadol 100mg/2ml (Tramol) + Inj. Dimenhydrinate 50mg/ml (Gravinate) dilute in 100ml 0.9% NS. x IV ☞ OR Inj. Nalbuphine 10mg/ml (Kinz) + Inj. Dimenhydrinate 50mg/ml (Gravinate) dilute in 100ml 0.9% NS. x IV ☞ With spasm: Inj. Drotaverine 40mg to 80mg (Nospa, Relispa) x dilute in 100ml 0.9% Normal saline x IV x STAT or put 1-2 ampule in R/L. ☞ Gastroprotective: Inj. Omeprazole 40mg (Risek, Ruling) x IV x STAT ☞ With vomiting – consider ONE of the following anti-emetics: ☞ Inj. Metoclopramide 10mg/2ml (Metaclon) x IV x TDS ☞ OR Inj. Dimenhydrinate 50mg/ml (Gravinate) x IV x TDS ☞ OR Inj. Ondansetron 8mg/4ml (Onset, Onseron) x diluted in 50 to 100 ml of 0.9% NS OR D5%W, IV over 15 minutes. ☞ IV antibiotics for secondary infection: Inj. Ceftriaxone 1-2g x IV x OD
Radiology: X-ray KUB, U/S KUB, CT KUB, <u>Intravenous pyelogram</u> (IVP)	

ACUTE PYLONEPHRITIS

Definition: Pylonephritis is an infection of the upper urinary tract. Acute pyelonephritis is infection of the renal parenchymal and pelvicalyceal system.

Clinical features

• Fever and chills
• Temperature greater than 100.4°F (38.0°C)
• Flank pain or costovertebral angle tenderness
• Irritative voiding symptoms (e.g., urgency, frequency, and dysuria)
• Abdominal (Suprapubic) pain
• Nausea, vomiting, & dehydration.

It is also critical to be aware of signs of sepsis (e.g., tachycardia, tachypnea, hypotension, fever or hypothermia, poor capillary refill, mottled or ashen skin, cyanosis, newly altered mental state, or reduced urine output).

The triad of flank pain, fever, and nausea and vomiting occurs much more often in patients with pyelonephritis than in those with cystitis.

Diagnostic workup

• CBC: leukocytosis, anemia
• Acute inflammatory markers: ESR or CRP – elevated
• Procalcitonin: Elevated
• Urinalysis: WBCs ≥10/HPF; red blood cells ≥5/HPF.
• Gram stain: typically, gram-negative rods; less typically gram-positive cocci.
• Urine culture: bacteria ≥100,000 colony-forming units (CFU)/mL
• Blood culture: any bacterial growth is considered abnormal
• Ultrasound KUB: gross structural abnormalities; hydronephrosis; stones; perirenal fluid collections
• Spiral CT scan with contrast: altered renal parenchymal perfusion; altered excretion of contrast; perinephric fluid; perirenal disease.
• MRI scan – suitable for those who are allergic to IV contrast dye

Rx

- Stabilize patients using ABCD&E approach.
- Establish large-bore intravenous (IV) access.
- Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂
- Obtained labs: CBC, BUN, Creatinine, electrolytes, LFTs, CRP/ESR, Blood sugar, calcium, uric acid level, urinalysis and urine C&S.
- IV fluid: Inj. Ringer Lactate 1L or 0.9%NS 1L x IV x OD/BD
- Empirical IV antibiotics therapy: Initially IV Antibiotics first 48-72 hours followed by 5-7 days of oral therapy (Tab. Ciprofloxacin 500mg x BD or Tab. Moxiget 400mg or Cap Cefspan 400mg x OD)
 - ↳ Inj. Ceftriaxone 1-2g (Oxidil, Rocephin) x IV x OD
 - ↳ OR Inj. Cefepime 1-2g (Uceph) x IV x TDS
 - ↳ OR Inj. Ciprofloxacin 400mg/100ml (Novidate, Ciplet DS) x BD
 - ↳ OR Inj. Piperacillin + Tazobactam 4.5g (Tanzo) x IV x TDS
 - ↳ OR Inj. Imipenem/Cilastatin 500mg (Cilapen, Tienam) x IV x TDS
- For fever: Inj. Paracetamol 1g/100ml (Provas) x IV x TDS
- Inj. Omeprazole 40mg (Risek) x IV x OD
- With spasm: Inj. Drotaverine 40mg to 80mg (Nospa, Relispa) dilute in 100ml 0.9% Normal saline x IV x stat or put 1-2 ampule in R/L.
- For pain/analgesia:
 - ↳ Inj. Paracetamol 1g/100ml (Provas, Paracet) x IV x TDS/SOS
 - ↳ OR Inj. Ketorolac 30mg/ml (Toradol) in 4ml 0.9% N/S x IV
- With vomiting – consider ONE of the following anti-emetics:
 - ↳ Inj. Metoclopramide 10mg/2ml (Metaclon) x IV x TDS
 - ↳ OR Inj. Dimenhydrinate 50mg/ml (Gravinate) x IV x TDS
 - ↳ OR Inj. Ondansetron 8mg/4ml (Onset, Onseron) x diluted in 50 to 100 ml of 0.9% NS OR D5%W, IV over 15 minutes.
- Radiology: X-ray KUB, US KUB, CT KUB, Intravenous pyelogram (IVP)
- Indications for hospitalization:
 1. Inability to maintain oral hydration or adherence to the medication regimen
 2. Hypotension
 3. Vomiting
 4. Dehydration
 5. Sepsis
 6. High WBC count
 7. Patients with a temperature >102.2°F (39.0°C)
 8. Severely ill patients with marked debility or multiple comorbidities
 9. Pregnancy
 10. Uncertainty about the diagnosis.

SEE NEPHROLOGY & UROLOGY FOR DETAILED MANAGEMENT

CARDIAC ARREST

Cardiac Arrest Management Protocol



Initial Response:

1. **Scene safety and initial assessment:**
 - » Ensure the scene is safe for both the responder and the patient.
 - » Check for responsiveness by tapping the patient and shouting, "Are you OK?"
2. **Activate emergency response system:**
 - » Call for emergency medical services (EMS) immediately or direct someone to do so.
 - » If an Automated External Defibrillator (AED) is available, retrieve it.
3. **Basic Life Support (BLS):**
 - » **Check pulse and breathing:**
 - ↳ Check for a carotid pulse (for no more than 10 seconds).
 - ↳ Look, listen, and feel for breathing. If there is no breathing or only gasping, assume cardiac arrest.
 - » **Begin Chest Compressions:**
 - ↳ Place the heel of one hand on the center of the chest (lower half of the sternum) and the other hand on top.
 - ↳ Interlock your fingers and ensure your shoulders are directly over your hands.
 - ↳ Compress the chest at least 2 inches deep (5 cm) at a rate of 100-120 compressions per minute.
 - ↳ Allow full chest recoil after each compression.
 - » **Ventilations:**
 - ↳ After 30 compressions, give 2 breaths using a bag-valve-mask (BVM) or mouth-to-mouth if no bag-valve-mask (BVM) is available.
 - ↳ Each breath should last about 1 second and cause visible chest rise.

Use of AED:

1. **Turn on the AED:** Follow the voice prompts and visual cues provided by the AED.
2. **Attach Pads:** Attach the adhesive AED pads to the patient's bare chest as indicated (one pad on the upper right side of the chest and the other on the lower left side).
3. **Analyze Rhythm:**
 - » Ensure no one is touching the patient.
 - » Allow the AED to analyze the heart rhythm.
4. **Shock Delivery:**
 - » If a shock is advised, ensure no one is in contact with the patient and deliver the shock.
 - » Immediately resume CPR starting with chest compressions after the shock.

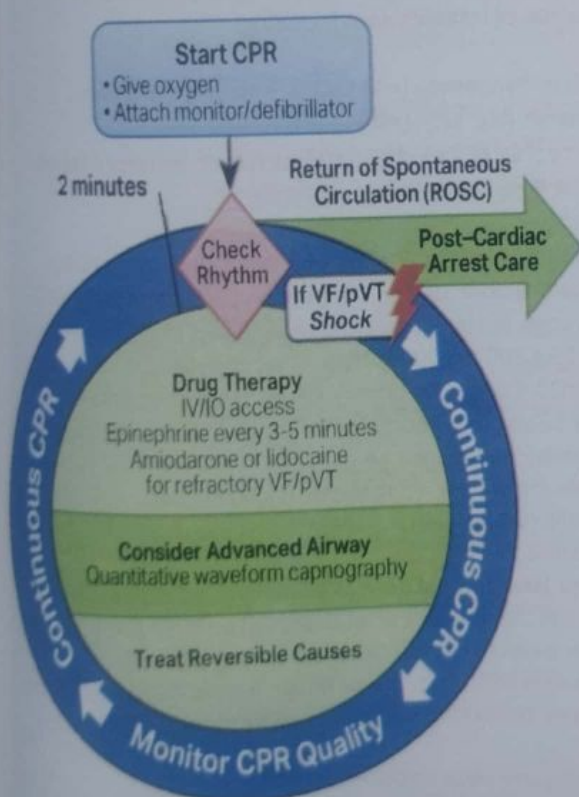
Advanced Life Support (ALS):

- » **Airway Management:**
 - ↳ Secure the airway using advanced techniques (e.g., endotracheal intubation, supraglottic airway).
 - ↳ Confirm proper placement and secure the device.
- » **Establish intravenous (IV) access**
- » **Medications:**
 - ↳ Administer Inj. Epinephrine (Adrenaline) 1mg IV every 3-5 minutes during cardiac arrest.
 - ↳ Consider administering Amiodarone or Lidocaine for refractory ventricular fibrillation or pulseless ventricular tachycardia.
- » **Identify and treat reversible causes of cardiac arrest:** e.g., hypoxia, hypovolemia, hyperkalemia, hypothermia, tension pneumothorax, cardiac tamponade, toxins, thrombosis.

Post-Cardiac Arrest Care:

- **Vitals monitoring:** Check BP, PR, RR, Temperature, SpO₂
- **Return of Spontaneous Circulation (ROSC):**
 - Optimize ventilation and oxygenation.
 - Maintain a target oxygen saturation of 94-99%.
 - Avoid hyperventilation; target a respiratory rate of 10-12 breaths per minute.
 - Monitor and manage hemodynamics (maintain a systolic blood pressure >90 mmHg or mean arterial pressure >65 mmHg).
- **Neurological Care:**
 - Perform a targeted temperature management (cooling) if indicated to improve CNS outcomes.
 - Monitor and treat seizures.
- **Coronary Reperfusion:** Consider immediate coronary angiography and percutaneous coronary intervention (PCI) if a cardiac cause of arrest is suspected.
- **Multidisciplinary Care:** Coordinate post-cardiac arrest care with a multidisciplinary team, including cardiologists, neurologists, and critical care specialists.

Adult Cardiac Arrest Circular Algorithm



CPR Quality

- Push hard (at least 2 inches [5 cm]) and fast (100-120/min) and allow complete chest recoil.
- Minimize interruptions in compressions.
- Avoid excessive ventilation.
- Change compressor every 2 minutes, or sooner if fatigued.
- If no advanced airway, 30:2 compression-ventilation ratio.
- Quantitative waveform capnography
 - If PETCO₂ is low or decreasing, reassess CPR quality.

Shock Energy for Defibrillation

- **Biphasic:** Manufacturer recommendation (eg, initial dose of 120-200 J); if unknown, use maximum available. Second and subsequent doses should be equivalent, and higher doses may be considered.
- **Monophasic:** 360 J

Drug Therapy

- **Epinephrine IV/IO dose:** 1 mg every 3-5 minutes
- **Amiodarone IV/IO dose:** First dose: 300 mg bolus. Second dose: 150 mg.
- **Lidocaine IV/IO dose:** First dose: 1-1.5 mg/kg. Second dose: 0.5-0.75 mg/kg.

Advanced Airway

- Endotracheal intubation or supraglottic advanced airway
- Waveform capnography or capnometry to confirm and monitor ET tube placement
- Once advanced airway in place, give 1 breath every 6 seconds (10 breaths/min) with continuous chest compressions

Reversible Causes

- Hypovolemia
- Hypoxia
- Hydrogen ion (acidosis)
- Hypo-/hyperkalemia
- Hypothermia
- Tension pneumothorax
- Tamponade, cardiac
- Toxins
- Thrombosis, pulmonary
- Thrombosis, coronary

Return of Spontaneous Circulation (ROSC)

- Pulse and blood pressure
- Abrupt sustained increase in PETCO₂ (typically ≥40 mm Hg)
- Spontaneous arterial pressure waves with intra-arterial monitoring

MYOCARDIAL INFARCTION/STEMI

CLINICAL FEATURES

- Acute retrosternal chest pain, dull and squeezing, radiating to left chest, arm, shoulder, neck, jaw, and/or epigastrium, often, worsened by exertion, stress, not relieved by nitrates, often peaking in the morning.
- Dyspnea, pallor, nausea, vomiting, diaphoresis, dizziness, and anxiety/Distress (sense of doom or death)



TREATMENT OF MYOCARDIAL INFARCTION/STEMI

- Stabilize patients using ABCD&E approach.
- Establish large-bore intravenous (IV) access.
- Monitoring and recording vital signs (BP, PR, RR, Temperature and SpO₂).
- Obtained investigation: CBC, BUN, Creatinine, Electrolytes, RBS, CRP, Lipid profile, serum troponin and other if indicated such as LFTs, LDH, NT pro-BNP or BNP, Chest x-ray, CT angiography and Echocardiography.
- Bedrest recommendation for at least 12 to 24 hours; thereafter, light activity if patient is stable.
- Make patient NPO: to prevent aspiration due to vomiting, except for sips of water until pain free and stable.
- IV fluids therapy: RL and 0.9% NS x IV x BD/TDS to maintain hydration and hemodynamic stability. Recommended maintenance dose around 30-35 ml/kg/day for adults. Adjust fluid therapy based on individual patient factors such as age, comorbidities (e.g., heart failure, renal impairment), and hemodynamic status.
- Glycemic control: If blood glucose is significantly elevated, an intravenous insulin infusion may need to be given, but rigid control has not been shown to be necessary as per local protocol for dosing guidelines.
 - Hypoglycemia: Manage, if blood glucose is < 60 mg/dL.
 - Hyperglycemia: Manage and keep blood glucose levels between 140 to 180 mg/dL (7.8 to 10.0 mmol/L).
- The standard protocol for ACS typically involves a combination of interventions including:
 - Immediate assessment of symptoms and risk factors.
 - Administration of oxygen: Give in patient with cyanosis or hypoxemia (<94 SpO₂) → Nasal O₂ at 2 L/min.
 - DUAL ANTIPLATELET THERAPY (DAPT) to ↓ vascular events (e.g. MI, stroke).
 - Tab. Aspirin 300mg (Disprin) one tablet per oral once (PO) or Tab. Aspirin 75mg (Loprin, Ascard) 4 tablets PO, once followed by Tab. Aspirin 75mg or 150mg at dose 75 – 150 mg once daily.
 - AND add one of the following:
 - Tab. Prasugrel 10mg (Eficlot, Obsoprel) at loading dose 60mg, PO, once on DAY1, then 10mg x OD.
 - OR Tab. Ticagrelor 90mg (Brilinta, Anplag) at loading dose 180mg, PO, once on DAY1, then 90mg x BD.
 - (Both above drugs demonstrated superior outcomes to clopidogrel in clinical studies of primary PCI.)
 - OR Tab. Clopidogrel 75mg (Lowplat) x loading dose 300 to 600mg, then 75mg once daily
 - Anticoagulate with Inj. Enoxaparin at dose 1mg/kg BD (OD if GFR <30mL/min), OR Inj. Heparin at dose 60 units/kg (max 4000 Units), IV bolus initially, followed by 12 units/kg/hour infusion (max of 1000 units), adjust dose to target aPTT 1.5–2.0 × control (about 50-70 seconds), until discharge
 - Nitrates: Provide rapid relief to pain if chest pain persists. Do not use if Systolic BP is < 90 mm Hg.
 - Glyceryl Trinitrate 0.4mg/dose (Nitril spray) 1 spray SL (Sublingually)
 - OR Tab. Glyceryl Trinitrate 0.5mg (Angised) x 1 tablet SL (Sublingually)
 - Analgesia for pain management: Inj. Morphine sulphate 10mg/ml x at dose of 4–8mg or Inj. Nalbuphine 20mg/ml (Kinz) at dose 10 to 20 mg, diluted in 0.9% NS x IV. Subsequent small doses can be given every 15 minutes until adequate pain control is achieved. Monitor patients for signs of respiratory depression.

Adjunct antiemetic therapy is recommended in combination with morphine or Nalbuphine to manage potential nausea and vomiting associated with opioid administration such as Inj. Metoclopramide 10mg/2ml (Metaclo) or Inj Dimenhydrinate 50mg/1ml (Gravinate) x IV.
 - Continuous cardiac monitoring: Cardiac monitor, Serial ECG and Serial troponin levels.
 - High dose Statins: Early initiation of high-intensity statin regardless of baseline cholesterol, LDL, and HDL levels.
 - Tab. Atorvastatin 40mg (Lipitor, Lipiget) x Once daily. **Dosage:** ≥ 40mg (upto 80mg/day)
 - OR Tab. Rosuvastatin 20mg (X-Plended, Rovista) x Once daily. **Dosage:** ≥ 20mg (up to 40mg/day)
 - Consider cardioprotective drugs as indicated:
 - Beta Blockers: reduces myocardial oxygen demand, (avoid in patients with hypotension, asthma, features of heart failure, and/or risk of cardiogenic shock). **Start low and increase slowly, monitoring pulse and BP.** Hold if systolic BP <100 mmHg, Heart rate <50 beat/minute.
 - Tab. Carvedilol 6.25mg (Carveda, Carlov) x started at a dose of 6.25mg orally twice daily and may be increased 12.5mg, and then 25mg BD. Available strength: 3.125mg, 6.25mg, 12.5mg and 25mg

Chapter
23

OR Tab. Metoprolol 25mg OR 50mg (Merol) x Tartrate initially 12.5mg orally every 6 hours, increase to 25 to 50mg every 6 hours as tolerated) in eligible patients, beginning within the 1st 24hr.

2. ACE inhibitors (or ARB) in all patients. Monitor renal function.

Consider in patients if any of the following are present:

1. ST segment elevation MI (STEMI) – especially in those patient with ECG finding of anterior MI.
2. Left ventricular EF $\leq 40\%$
3. Patient with Hypertension
4. Patient with Heart failure
5. Patient with Diabetes mellitus

Tab. Lisinopril 5mg or 10mg (Zestril, Trupril) 2.5mg up to 5mg x OD titrated at target dose 10mg x OD

OR ARBs, if contraindication to ACEIs (Dry cough, angioedema): Tab. Valsartan 160mg (Exforge, Diovan) x Twice daily (BD) is equivalent to captopril in reducing mortality.

3. Do an echo to assess LV ejection fraction (LVEF). Add aldosterone antagonist (eg spironolactone) if LVEF $< 40\%$.

Gastroprotective: Inj. Pantoprazole 40mg/vial (Zopent) x IV x OD

Stool softener: Syp. Lactulose (Duphalac) 30ml x HS or Skilax drops up to 10 – 20 drops in a half cup water x OD

Anxiolytic or hypnotic if needed: Alprazolam, lorazepam, or diazepam

Reperfusion Therapy: Percutaneous coronary intervention (PCI) preferable over Fibrinolytic therapy

1. Primary PCI with stenting is the treatment of choice, should be done, if available within 90 minutes and if primary PCI is unavailable within < 120 minutes $\rightarrow$ Fibrinolytic therapy.

2. Fibrinolytic therapy:

OR Inj. Alteplase 50mg/vial (Actylise) at dose in patients weight > 67 kg: 15mg initial IV bolus; 50mg infused over next 30 minutes; 35mg infused over next 60 minutes and in those weight < 67 kg: 15mg initial IV bolus; 0.75mg/kg infused over next 30 minutes; 0.5mg/kg infused over next 60 minutes.

OR Inj. Reteplase 18 mg (Retelex) x Double bolus at dose 10 units IV over 2 minute followed by 10 units IV bolus 30 minutes later.

OR Inj. Tenecteplase 40mg (TNkase) x Single bolus dose

Dosing of Tenecteplase based on weight per kg:

Weight/kg	Dose in mg	Dose to be given in ml
< 60 kg	30 mg	6 mL
≥ 60 but < 70 kg	35 mg	7 mL
≥ 70 but < 80 kg	40 mg	8 mL
≥ 80 but < 90 kg	45 mg	9 mL
≥ 90 kg	50 mg	10 mL

OR Inj. Streptokinase 1.5 million units (MU) in 100 mL of 5% Dextrose in water (D5%W) OR 0.9% NS given IV over 60 minutes.

FIBRINOLYTIC THERAPY

Indications

1. STEMI: ST elevation of > 2 mm in 2 or more chest leads or ST elevation of > 1 mm in 2 or more limb leads
2. New or presumed new left bundle branch block with symptoms consistent with MI.
3. Posterior wall myocardial infarction, as evidenced by dominant R waves and ST depression in leads V1–3
4. Absence of contraindications.

Contraindications

Absolute Contraindications:

- Active bleeding (menses excluded)
- Prior hemorrhagic stroke, ischemic stroke within 3 months, except acute ischemic stroke within 3 – 4.5 hours
- Intracranial or spinal cord neoplasm or arteriovenous malformation
- Suspected aortic dissection or pericarditis
- Closed head or facial trauma within 3 months

Relative Contraindications:

- Severe, uncontrolled BP ($> 180/110$ mmHg)
- History of chronic, severe, poorly controlled hypertension
- Anticoagulation with therapeutic or elevated international normalized ratio ($> 2-3$)
- Old ischemic stroke (> 3 months ago)
- Intracerebral disease other than above
- Recent (< 3 weeks) major trauma/surgery
- Prolonged CPR (> 10 min)
- Known bleeding diathesis.
- Recent internal bleeding (within 2–4 week)
- Active peptic ulcer disease
- Recent noncompressible vascular punctures (including subclavian and internal jugular central lines)
- Pregnancy/childbirth
- Patients treated previously with streptokinase shouldn't receive streptokinase a second time.

Revascularization: All patients with suspected acute coronary syndrome should be considered for emergency percutaneous coronary intervention (PCI). Patients with multivessel disease may be considered for CABG instead of PCI

Consider dual antiplatelet therapy after PCI with stent placement for at least 12 months.

PULMONARY EDEMA

Diagnostic approach

- ✓ **Clinical Assessment:**
 - » **History:** Obtain a thorough patient history, focusing on symptoms such as sudden onset of dyspnea (shortness of breath), orthopnea (difficulty breathing while lying flat), paroxysmal nocturnal dyspnea (sudden nighttime shortness of breath), cough (with or without frothy sputum), chest pain, and fatigue.
 - » **Physical Examination:** Look for signs such as tachypnea (rapid breathing), tachycardia (rapid heart rate), hypertension or hypotension, jugular venous distension, crackles/rales on lung auscultation, wheezing, and peripheral edema (swelling of the extremities).
- ✓ **Diagnostic workup**
 - » **Chest X-ray:** Typically shows bilateral pulmonary infiltrates, indicating fluid accumulation in the lungs.
 - » **ECG:** Helps identify arrhythmias, ischemia, or myocardial infarction as underlying causes.
 - » **Echo:** Assesses cardiac function and identifies structural heart abnormalities or valvular issues.
 - » **Obtained blood tests:** CBC, electrolytes, BUN, Creatinine, LFTs, serum troponin, BNP or NT-proBNP levels to evaluate heart failure and ABGs to assess oxygenation and acid-base status.
 - » **Pulmonary Function Tests (if applicable):** May help differentiate pulmonary from cardiac causes.



TREATMENT OF PULMONARY EDEMA

- ✓ **Stabilize patients using ABCD&E approach.**
 - » **Positioning:** Elevate the head of the bed to reduce venous return and improve breathing.
 - » **Administer supplemental oxygen** to maintain oxygen saturation (SpO₂) > 92%. Use non-invasive positive pressure ventilation (NIPPV) like CPAP or BiPAP if severe respiratory distress or hypoxia persists.
- ✓ **Establish intravenous (IV) access.**
- ✓ **Vitals monitoring:** Check BP, PR, RR, Temperature, SpO₂
- ✓ **Obtained labs:** CBC, BUN, Creatinine, Electrolytes, LFTs, Blood sugar, Cardiac enzyme and ABGs
- ✓ **Medications:**
 - » **Administer IV loop diuretics to reduce fluid overload:**
 - ✎ **Inj. Furosemide 20mg/2ml (Lasix)** at dose 20-40 mg IV bolus, may be repeated or increased by 20 mg/dose every 1-2 hours until urine output increases and dyspnea improve. Subsequent doses can be doubled every 2 hours if there is no response, up to a maximum of 200 mg IV. **Continuous infusion:** 0.1 mg/kg/hr to 1 mg/kg/hr if bolus doses are ineffective. Monitor urine output and electrolytes.
 - » **Vasodilators:** Use nitrates (nitroglycerin) to decrease preload and afterload, improving cardiac output and reducing pulmonary congestion. Monitor blood pressure closely.
 - ✎ **Glyceryl Trinitrate 0.4mg/dose (Nitrl spray)** 1 spray SL (Sublingually) OR **Tab. Glyceryl Trinitrate 0.5mg (Angised)** x 1 tablet SL (Sublingually) every 5 minutes as needed, up to 3 doses.
 - ✎ **IV nitrates infusion:** Start at 10-20 µg/min and titrate up by 5-10 µg/min every 5-10 minutes based on response and blood pressure, up to 200 µg/min.
 - » **Morphine** to reduce anxiety and venous return
 - ✎ **Inj. Morphine sulphate 10mg/ml** x at dose of 4—8mg OR **Inj. Nalbuphine 20mg/ml (Kinz)** at dose 10 to 20 mg, diluted in 0.9% NS x IV. Subsequent small doses can be given every 15 minutes until adequate pain control is achieved. Monitor patients for signs of respiratory depression.
 - ✎ **Adjunct antiemetic therapy** is recommended in combination with morphine or Nalbuphine to manage potential nausea and vomiting associated with opioid administration such as **Inj. Metoclopramide 10mg/2ml (Metaclo)** or **Inj. Dimenhydrinate 50mg/1ml (Gravinate)** x IV.
 - » **Inotropes (if needed):** In cases of cardiogenic shock or severe heart failure to improve cardiac contractility.
 - ✎ **Dobutamine** at initial dose: 2-5 µg/kg/min IV. Titrate up to 20 µg/kg/min based on clinical response.
 - ✎ **Milrinone** at loading dose: 50 µg/kg IV over 10 min. **Maintenance infusion:** 0.375-0.75 µg/kg/min IV.
- ✓ **Identify and treat underlying cause:**
 - » **Myocardial Ischemia/Infarction:** Administer antiplatelet agents (e.g., aspirin), anticoagulants (e.g., heparin), and consider urgent revascularization (e.g., percutaneous coronary intervention) see MI treatment
 - » **Hypertension:** Control blood pressure with appropriate antihypertensive medications.
 - » **Treat significant arrhythmias** with antiarrhythmic medications or electrical cardioversion if necessary.
 - » **Valvular Disease:** Surgical or percutaneous intervention may be required for severe valvular abnormalities.

PULMONARY EMBOLISM

Wells' Criteria for Pulmonary Embolism

The Wells score is a diagnostic algorithm for assessing the probability of PE and has been validated in inpatient and outpatient settings.

Criteria features	Points
✓ Clinical symptoms of deep venous thrombosis (DVT)	3
✓ PE more likely than other diagnoses	3
✓ Previous pulmonary embolism or deep venous thrombosis (DVT)	1.5
✓ Tachycardia (Heart rate > 100/min)	1.5
✓ Surgery or immobilization in the past 4 weeks	1.5
✓ Hemoptysis	1
✓ Malignancy/cancer	1
Original Wells score (clinical probability)	
✓ Total score 0–1: low probability of PE (6%)	
✓ Total score 2–6: moderate probability of PE (23%)	
✓ Total score ≥ 7: high probability of PE (49%)	
Modified Wells score (clinical probability)	
✓ Total score ≤ 4: PE unlikely (8%)	
✓ Total score > 4: PE likely (34%)	

Revised Geneva score

The revised Geneva score utilizes objective clinical variables. It has been externally validated and was initially studied in emergency department outpatients.

Criteria	Points
✓ Age > 65 years	1
✓ Prior history of DVT or PE	3
✓ Recent surgery or fracture of the lower limbs	2
✓ Personal history of cancer	2
✓ Unilateral lower limb pain	3
✓ Hemoptysis	2
✓ Heart rate 75–94/min	3
✓ Heart rate ≥ 95/min	5
✓ Pain on palpation of lower limb and unilateral edema	4

Clinical pretest probability

- ✓ Total score < 4: low probability of PE (9%)
- ✓ Total score 4–10: intermediate probability of PE (26%)
- ✓ Total score > 10: high probability of PE (76%)

Stepwise Diagnostic approach

- ✓ Assess for hemodynamic stability.
 - » Stable patients: systolic BP > 90 mmHg
 - » Unstable patients: systolic BP < 90 mmHg for > 15 minutes, evidence of shock, or BP drop > 40 mmHg for > 15 minutes
- ✓ Assess the pretest probability of Pulmonary Embolism
 - » Low: modified Wells score for PE ≤ 4, Wells score for PE < 2, or revised Geneva score < 4
 - » Intermediate: modified Wells score for PE ≤ 4, Wells score for PE 2–6, or revised Geneva score 4–10
 - » High: modified Wells score for PE > 4, Wells score for PE > 6, or revised Geneva score > 10
- ✓ Obtain D-dimer.
 - » D-dimer ≥ 500 ng/mL: CTPA or V/Q scan
 - » D-dimer < 500 ng/mL: PE is unlikely; consider other causes of symptoms
 - » Unstable patients and/or high probability of PE: Obtain CTPA or V/Q scan for a definitive diagnosis.
 - » Critically ill patients who cannot be safely transported: bedside echocardiography
 - » High sensitivity and negative predictive value: A negative D-dimer test most likely rules out PE.
 - » Low specificity: positive results in all forms of fibrinolysis

Clinical presentation

Acute onset of symptoms, often triggered by a specific event (e.g., on rising in the morning, sudden physical strain/exercise)

1. Respiratory Symptoms:

- » **Dyspnea:** Sudden SOB.
- » **Tachypnea:** Rapid breathing.

2. Cardiac Symptoms:

- » **Chest Pain:** Often pleuritic (worsens with breathing) but can be non-specific.
- » **Palpitations:** Feelings of rapid or irregular heartbeat.

3. Systemic Symptoms:

- » **Hemoptysis:** Coughing up blood.
- » **Syncope:** Fainting or loss of consciousness.

4. Signs of Right Heart Strain:

- » **Jugular Venous Distension (JVD):** Elevated jugular veins, especially in severe cases.
- » **Hypotension:** Low BP potentially leading to shock.

5. Additional Findings:

- » **Cyanosis:** Bluish discoloration of lips or extremities.
- » **Low-grade fever**
- » **Leg Swelling:** Indicative of deep vein thrombosis (DVT), which may be associated with PE.

6. Features of massive PE: syncope and obstructive shock with circulatory collapse (due to a saddle thrombus)

7. Features of PE under anesthesia during surgery

- » Increasing heart rate
- » Drop in blood pressure
- » Drop in partial pressure of end-tidal CO₂ (PetCO₂) in capnography.
- » Drop in PaO₂ saturation end.

PE Clinically suspicion patient don't wait for investigation

TREATMENT OF PULMONARY EMBOLISM (PE)**1. Stabilize patients using ABCD&E approach.****2. Establish intravenous (IV) access.**

3. Vitals monitoring: BP, PR, RR, Temperature, Check SpO₂ & Give high flow O₂ as appropriate. Use nasal cannula, face mask, or non-rebreather mask

4. Gentle bolus IV fluid: Inj. 0.9% NS ≤500mL x IV x STAT. Avoid volume overload, which may be harmful in cases of right ventricular strain

5. Obtained investigations: CBC, BUN, creatinine, electrolytes, LFTs, Blood sugar, D-dimers level, cardiac troponin, BNP and ABGs.

Imaging: Chest x-ray, CT pulmonary angiography (CTPA)—most definitive test, Echocardiography, Ventilation/perfusion scintigraphy (V/Q scan), Lower extremity venous ultrasound, Pulmonary angiography

6. Provide analgesia; avoid NSAIDs if possible.

Inj. Nalbuphine 10-20mg (Kinz) + with Inj. Dimenhydrinate 50mg/ml (Gravinate) dilute in 8ml 0.9% N/S x give slow IV

OR Inj. Morphine 10mg/ml diluted in 10ml 0.9% N/S x 2mg x IV STAT.

7. Anticoagulation therapy (LMWH)**A. Low molecular weight heparin or Unfractionated Heparin (UFH):**

- » **LMWH** such as Inj. Enoxaparin sodium 80mg/0.8ml (Clexane) at dose 1 mg/kg subcutaneously (SC) every 12 hours. **Alternative Dose:** 1.5 mg/kg subcutaneously (SC), once daily, depending on patient characteristics and renal function.

- » **UFH** (if LMWH is contraindicated or renal function is impaired):

↳ **Bolus dose:** 60-80 units/kg IV bolus (maximum 5,000 units).

↳ **Infusion dose:** 12-18 units/kg/hour IV infusion, adjusted based on aPTT (activated partial thromboplastin time).

B. Direct oral anticoagulants (DOACs) such as Rivaroxaban or Apixaban
For bridging to long-term therapy

- » **Tab. Rivaroxaban (Revaxo, Xcept)**

↳ **Initial Dose:** 15 mg orally twice daily for 21 days.

↳ **Maintenance Dose:** 20 mg orally once daily.

- » **Tab. Apixaban:**

↳ **Initial Dose:** 10 mg orally twice daily for the first 7 days.

↳ **Maintenance Dose:** 5 mg orally twice daily.

2. Thrombolysis

- » **Indication:** Severe PE with hemodynamic instability or massive PE.

- » **Tissue Plasminogen Activator (tPA) (e.g., Alteplase):**

↳ **Dose:** 100 mg IV over 2 hours.

↳ **Alternative Regimen:** 50 mg IV bolus, followed by 50 mg IV over the next 2 hours (for some protocols).

8. Consider vasopressors, if hypotension (systolic BP is <90 mmHg) persists despite fluid resuscitation: Inj. Norepinephrine at dose: 0.1-0.5 mcg/kg/min IV infusion, titrated to blood pressure response.

9. Consideration of Surgical or Catheter-Based Interventions: Pulmonary Embolism Response Team (PERT) Consultation → **Indication:** For severe cases where mechanical thrombectomy or catheter-directed thrombolysis might be considered.

10. General care

- » Monitor pupillary reflexes and record GCS level
- » Avoid NSAIDs if patient receiving anticoagulation or thrombolytics
- » Identify and treat underlying cause

FEVER WITH ALTERED LEVEL OF CONSCIOUSNESS (ALOC)

Detailed History:

- » Onset and duration of symptoms
- » Past medical history, including any chronic conditions or recent illnesses
- » Medication history, including prescription and over-the-counter drugs
- » Travel history, exposure to infectious diseases, and recent vaccinations
- » Occupational and environmental exposures

Physical Examination:

- » Assessment of vital signs, including temperature, blood pressure, heart rate, and respiratory rate
- » Neurological examination to assess level of consciousness, pupillary response, motor and sensory function, and signs of meningeal irritation
- » Examination of other organ systems to identify any focal signs of infection or systemic illness.

Laboratory Investigations: Obtained Complete blood count (CBC) with differential to assess for leukocytosis or leukopenia. BUN & creatinine for renal function. Serum electrolytes to evaluate electrolyte abnormalities. LFTs to assess liver function. Thin and thick blood smear to rule out malaria.

- » Blood cultures to identify the presence of bacteremia or sepsis
- » Arterial blood gas (ABG) analysis to assess for acid-base disturbances and oxygenation status
- » Lumbar puncture (if meningitis, encephalitis is suspected) for CSF analysis, CSF culture and CSF PCR.

Radiological Studies: CT scan or MRI brain to evaluate for structural abnormalities, intracranial hemorrhage, or space-occupying lesions. Chest X-ray or CT chest to assess for pneumonia or pulmonary infections.

Additional Tests:

- » Electrocardiogram (ECG) to evaluate for cardiac arrhythmias or ischemia
- » Toxicology screening if drug overdose or poisoning is suspected
- » Lumbar puncture and CSF analysis if central nervous system infection is suspected

The differential diagnosis for fever with altered level of consciousness (ALOC) includes:

☞ Central nervous system infections:

- » Meningitis
- » Encephalitis
- » Brain abscess

☞ Systemic infections:

- » Septicemia/sepsis
- » Cerebral Malaria
- » Typhoid fever

☞ Metabolic Disorders:

- » Diabetic ketoacidosis (DKA)
- » Hyperosmolar hyperglycemic state (HHS)
- » Hyponatremia

☞ Neurological Disorders:

- » Stroke
- » Status epilepticus
- » Intracranial hemorrhage

☞ Toxicological Causes:

- » Drug overdose
- » Alcohol intoxication
- » Carbon monoxide poisoning

☞ Other Causes:

- » Heat stroke
- » Hypoxic respiratory failure
- » Hypertensive encephalopathy

Rx

- ☞ Stabilize patients using ABCD&E approach.
- ☞ Establish large-bore intravenous (IV) access.
- ☞ Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂
- ☞ Obtained labs: CBC, BUN, Creatinine, Electrolytes, LFTs, RBS, PT, INR, MP ICT, ABGs, CSF analysis, CSF culture and CSF PCR.
- ☞ IV Crystalloid fluid: R/L, D5%W &/or 0.9% N/S 1L x IV x BD/OD
- ☞ Start empiric antibiotic therapy if bacterial infection is suspected:
 - ☞ Inj Ceftriaxone 2g (Oxidil, Rocephin,) x IV x BD
- ☞ With fever: Inj Paracetamol 1g/100ml (Provas) x IV x TDS
- ☞ Adjunct antiviral: Inj. Acyclovir 500mg (Acyclovir, Aclovir) x IV x TDS
Dosages: 10 mg/kg every 8 hourly for 10-14 days)
- ☞ Adjunct antimalarial: Inj. Artemisinin 60mg or 120mg (Gen-M)
Dosage: 2.4mg/Kg at 0, 12 and 24 hours then 2.4mg/Kg daily for upto 7 days. (For Dilution see above falciparum malaria)
- ☞ Gastroprotective: Inj. Omeprazole 40mg (Ruling, Risek) x IV x OD
- ☞ With seizures: Give Inj. Diazepam 10mg/2ml (Valium) x 10mg diluted in 8ml 0.9% NS OR D5%W x at dose 2mg up to 10mg x IV. For seizures prophylaxis: Inj. Levetiracetam 500mg/5ml (Lerace, Epilapsa) at dose 1-2g in 100ml 0.9% NS x IV over 15-20 minutes.
- ☞ Symptomatic Management: Treat associated symptoms such as headache, nausea, or pain as appropriate.
- ☞ Pass nasogastric (NG) tube and foley's catheter with attach bag.
- ☞ Encourage oral feeding.
- ☞ Identify and treat underlying cause.
- ☞ Monitor pupillary reflexes and GCS level.

STATUS MIGRAINOSUS

- ☞ **Definition:** Status migrainosus is a severe and prolonged form of migraine headache in a patient with a known migraine diagnosis (with or without aura). It's characterized by intense, debilitating head pain that lasts for > 72 hours and is often resistant to standard migraine treatments and often related to medication overuse.
- ☞ **Clinical features:** Symptoms may include severe head pain, nausea, vomiting, sensitivity to light and sound, and sometimes aura symptoms like visual disturbances. It can significantly impair daily functioning and may require medical intervention, such as intravenous medications, to alleviate symptoms and prevent complications.



TREATMENT OF STATUS MIGRAINOSUS

1. Initial Assessment:

- ☞ Confirm the diagnosis of status migrainosus based on clinical presentation and history.
- ☞ Exclude serious conditions that may mimic migraine, such as ICH or meningitis, if warranted.
- ☞ Consider CT brain plain or MRI brain.
- ☞ Establish large-bore intravenous (IV) access.

2. Acute Treatment: Stepwise therapy with reassessment between drug administration.

- ☞ **IV fluid therapy:** Administer 0.9% normal saline 500-1000 mL x IV STAT, over 30 minutes to an hour.
- ☞ **IV Antiemetic:** Inj. Metoclopramide 10mg/2ml (Maxolon, Metaclo) x at dose 10-20 mg IV x once
- ☞ **IV NSAIDs:** Inj. Ketorolac 30mg/ml (Toradol, Ketor) at dose 30-60mg, diluted in 8ml 0.9%NS x IV x once

3. Rescue Therapies: if initial acute treatments are ineffective, consider rescue therapies.

- ☞ Inj. Dexamethasone 4mg/ml (Decadron) at dose 8-12 mg IV x once
- ☞ Inj. Dihydroergotamine 1mg/ml x IM/SC: repeat every hour as needed; maximum 3 mg/day.
- ☞ **IV Anti-convulsants:** Inj. Sodium valproate 500mg/5ml (Epival) at dose 500-1000mg, OR Inj. Lacosamide 200mg/20ml (Lalap, Lacolet) x diluted in 100ml 0.9% NS x IV once, over 20 minutes.
- ☞ **IV Triptans:** Inj. Sumatriptan 6mg/0.5ml (Imigran) x at dose 4-6mg x subcutaneously (SC), may repeat once after 2 hour if needed. (Maximum dose: 12mg/day)
- ☞ **Adjunctive therapy:** Consider IV magnesium sulfate under specialist guidance: Inj. Magnesium sulphate 500mg/ml (5g/10ml) at dose 1-2g diluted in 100ml 0.9% NS x IV over 30 minutes

4. Migraine cocktail if unresponsive: Consider Migraine cocktails typically a combination of medications as listed above aimed at relieving acute migraine symptoms and preventing recurrence tailored to the patient's needs.

5. Monitoring:

- ☞ Monitor vital signs (BP, PR, RR, Temperature, SpO2), neurologic status, and response to treatment closely.
- ☞ **Assess for signs of complications:** serotonin syndrome (if using triptans), or assessment of dehydration.
- ☞ Avoid frequent use of opioids due to the risk of rebound headaches and medication overuse headache.
- ☞ Reduce light/noise in the patient's environment.

6. Preventive Strategies: Once the acute episode is resolved, initiate preventive measures to reduce the frequency and severity of future migraines. This may include:

- ☞ **Lifestyle modifications:** stress management, regular sleep patterns, dietary adjustments.
- ☞ **Pharmacologic prophylaxis (see – migraine headache Neurology section):** Propranolol, Flunarizine, Valproic acid, amitriptyline, pizotifen or CGRP (calcitonin gene-related peptide) monoclonal antibodies.
- ☞ Consider referral to a headache specialist for further evaluation and management.

7. Patient Education and Follow-up:

- ☞ Provide education about migraine triggers, lifestyle modifications, and the importance of adhering to the prescribed treatment plan.
- ☞ Schedule follow-up appointments to assess treatment response, adjust medications if necessary, and address any concerns or complications.
- ☞ **Multidisciplinary Approach:** Collaborate with other healthcare professionals, such as neurologists, pain specialists, psychologists, and physical therapists, as needed for comprehensive management.

BACTERIAL MENINGITIS

CLINICAL FEATURES

- Classic triad of meningitis: fever, headache, and neck stiffness.
- Altered mental status.
- Photophobia
- Nausea, vomiting
- Malaise
- Seizures
- Possibly cranial nerve palsies
- In the case of *Neisseria meningitidis*: Myalgia and, possibly, petechial, or purpuric rash

DIAGNOSTIC WORKUP

- CBC: Leukocytosis, anemia, thrombocytopenia
- Inflammatory marker: CRP – Elevated
- BUN & Creatinine: to assess renal function
- Serum electrolytes: Deranged ↓ Ca/Mg
- LFTs: to assess liver functions
- Blood glucose/RBS: ↓ or ↑
- Coagulation profile: Evidence of DIC
- Serum procalcitonin: Normal or elevated
- Blood Culture: (2SETS): Obtain before starting antibiotic therapy – Positive.
- Chest X-ray: may show pneumonia.
- CT scan brain: Normal or raised ICP.
- Lumber puncture for CSF studies

Bacterial Meningitis CSF analysis

Appearance	Cloudy, purulent fluid
Cell count	WBC > 1000/mm ³ , Pleocytosis Leucocyte Granulocytes ↑
Lactate	↑↑
Protein	↑ >1.5 g/L; (N <0.5 g/L).
Glucose	↓ <45 mg/dL, or <40%

- CSF culture – Positive
- CSF Gram stain – Positive
- CSF PCR – Positive (useful in distinguishing bacterial from viral meningitis).



- Stabilize patients using ABCD&E approach.
- Establish large-bore intravenous (IV) access.
- Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂
- Obtained labs: CBC, BUN, Creatinine, Electrolytes, LFTs, RBS, coagulation profile, ABGs, CSF analysis, CSF culture and CSF PCR.
- IV Crystalloid fluid as needed: D5%W x 1L x IV x OD, Ringer Lactate (RL) or Inj 0.9% N.S x 1L x IV x OD/BD
- Adjunct steroids: Ideally, adjuvant dexamethasone should be given with or shortly before the first dose of IV antibiotics in all previously well and non-immunosuppressed adults. However, it may be given within 4 hours of the first dose of antibiotics.
 - Inj. Dexamethasone 4mg/ml (Decadron) x 10mg STAT before starting antibiotics than 10mg every 6 hour for 4 days.
- EMPIRIC ANTIBIOTIC THERAPY:
 - Inj. Vancomycin 500mg (Vancomycin, Vanjec) at dose 15-20 mg/kg x IV TDS/BD (every 8-12 hours)
 - PLUS Inj. Ceftriaxone 2g (Rocephin, Oxidil) x IV x twice daily (BD), change antibiotics based on CSF culture.
OR Meropenem 1g (Meronem) at dose 1-2 g x IV x TDS
 - With fever: Inj. Paracetamol 1g/100ml (Provas) x IV x TDS
 - Gastroprotective: Inj. Omeprazole 40mg (Ruling) x IV x OD
 - With seizures: Give Inj. Diazepam 10mg/2ml (Valium) x 10mg diluted in 8ml 0.9% NS OR D5%W x at dose 2mg up to 10mg x IV.
For seizures prophylaxis: Inj. Levetiracetam 500mg/5ml (Lerace, Epilapsa) at dose 1-2g in 100ml 0.9% NS x IV over 15-20 minutes.
 - Symptomatic Management: Treat associated symptoms such as headache, nausea, or pain as appropriate.
 - Pass nasogastric (NG) tube and foley's catheter with attach bag.
 - Encourage oral feeding.
 - Identify and treat underlying cause.
 - Monitor pupillary reflexes and GCS level.

Duration of antibiotics therapy after L.P

- N. meningitidis (Meningococcal): 7 days
- H. influenzae: 7-10 days
- S. pneumoniae (Pneumococcus): 10-14 days
- Streptococcus agalactiae (group B streptococci): 14-21 days
- Unknown cause: 14 Days

RECOMMENDED DOSES FOR ANTIMICROBIALS USED TO TREAT SUSPECTED OR CONFIRMED BACTERIAL MENINGITIS

Antimicrobial	Dose	Maximum dose
Ceftriaxone	2 grams IV every 12 hours	4g/day
Cefotaxime	2 grams IV every 4-6 hours	12 g/day
Vancomycin	15-20 mg/kg IV every 8-12 hours (dosing based on actual body weight)	12 g/day
Ampicillin	2 grams IV every 4 hours	24 M.U/day
Penicillin G	2-4 million units every 4-6 hours	6 g/day
Meropenem	2 grams IV every 8 hours	

VIRAL MENINGITIS

△ Viral meningitis

C/C:

- » Classic triad of meningitis
- » Prodrome with flu-like syndrome
- » Low-grade fever
- » Malaise, fatigue & Myalgia
- » Upper respiratory symptoms
- » Altered mental status
- » Photophobia
- » Nausea, vomiting
- » Seizures
- » Possibly cranial nerve palsies

Investigation:

- » Routine test
 - CBC
 - BUN/Urea
 - Serum creatinine
 - Serum electrolytes
 - LFTs
 - Blood glucose
 - PT APTT & INR
- » L.P for CSF D/R, CSF C/S and PCR
- » Blood Culture & sensitivity
- » Chest X-ray (CXR)
- » CT scan brain

Viral meningitis CSF Study	
Appearance	Clear fluid
Cell count	Leukocyte 10-500/mm ³ Lymphocytes ↑
Lactate	Variable
Protein	Normal OR ↑
Glucose	Normal

Recommended empiric antiviral agent:
Acyclovir – Continue treatment if either HSV or VZV is detected, otherwise discontinue.



1. Airway:

- » Ensure patient is maintaining own airway
- » Assess and secure stable airway

2. Breathing: Check SpO₂ & Give high flow O₂ as appropriate

3. Circulation:

- » Maintain intravenous line (IV cannula)
- » Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂
- » Send labs: CBC, Blood sugar, BUN/Urea, Electrolytes, Creatinine, LFTs PT&INR, & ABGs.
- » Antiviral: Inj. Acyclovir 500mg (Acyclovir, Aclovir) x IV x TDS
 - ↳ Dosage: 10 mg/kg every 8 hourly for 10-14 days
- » Pearls & Pitfalls: If patients appear seriously ill and if acute bacterial seems possible (even if viral meningitis is suspected), appropriate antibiotics and corticosteroids are started immediately (without waiting for test results) and continued until bacterial meningitis is ruled out (i.e. no bacteria grow in CSF cultures). Web: Mark manuals/neurological diseases
 - ↳ Inj. Dexamethasone 4mg/ml (Decadron) 8mg x IV stat before starting antibiotics than 8 mg 6 hourly for 4 days
- » IV fluid if needed: D5%W x 1L x IV x OD, Ringer Lactate (RL) or Inj 0.9% N.S x 1L x IV x OD/BD
- » Gastroprotective: Inj. Omeprazole 40mg (Ruling, Risek) x IV x OD
- » With seizures: Give Inj. Diazepam 10mg/2ml (Valium) x 10mg diluted in 8ml 0.9% NS OR D5%W x at dose 2mg up to 10mg x IV.
For seizures prophylaxis: Inj. Levetiracetam 500mg/5ml (Lerace, Epilapsa) at dose 1-2g in 100ml 0.9% NS x IV over 15-20 minutes
Give Inj Diazepam (Valium) 10mg/2ml x diluted in 8ml 0.9% NS OR D5%W x (2mg upto 10mg) x IV

4. Disability & Exposure

- » Monitor pupillary reflexes and GCS level
- » Consider early HDU/ICU Admission
- » Pass Nasogastric tube and foley's catheter
- » Correct underlying cause
- » Treatment with acyclovir should be started in all patients who present with typical clinical signs of viral meningoencephalitis and only discontinued after PCR and antibody tests are negative for HSV and VZV, even if CSF is initially normal.

TUBERCULOUS MENINGITIS (TBM)

Pathogen: *Mycobacterium tuberculosis*

Incubation period: approximately 2–8 weeks

Risk factors: immunocompromised (HIV infection)

Clinical course

- Subacute course over several weeks or months
- Gradual manifestation with intermittent fever

Clinical features

- Typical symptoms of meningitis, including fever, headache, neck stiffness, and altered mental status
- Focal neurological deficits (e.g., hemiparesis) due to hematogenous dissemination of cranial arteritis
- Cranial nerve deficits; are most commonly seen in basal meningitis & predominantly involve the VI CN

Complications

- Communicating (malabsorptive) hydrocephalus
- Pituitary gland insufficiency

Diagnostic workup

Routine test

- CBC
- BUN/Urea
- Serum creatinine
- Serum electrolytes
- LFTs
- Blood glucose
- PT/APTT & INR

Perform lumbar puncture (LP)

- CSF analysis
- CSF culture and sensitivity – Gold standard for diagnosis, but results may take weeks.
- CSF analysis of adenosine deaminase (ADA) activity: $\uparrow\uparrow$

Chest X-ray

CT scan/MRI brain: possible hydrocephalus, basilar meningeal thickening, tuberculomas, edema, infarcts

TB MENINGITIS CSF STUDY

Appearance	Fibrin web
Cell-count	$\uparrow\uparrow\uparrow$ (10-1000/mm ³)
Cell-type	Lymphocytes
Glucose	$\downarrow\downarrow$ <1/2 of plasma
Protein	$\uparrow$ 1-5 g/L
Investigation of choice	CSF for Acid fast Bacilli (Z-N STAINING)



TREATMENT OF TUBERCULOUS MENINGITIS (TBM)

Management approach

- Isolation:** Every patient diagnosed with active tuberculosis must be isolated.
- After 1 month of ATT mycobacterium is absent from sputum and patient become non-infective. Restart full treatment if there is an interruption of $\geq$ 14 days during the intensive phase.

- First-line ATT is safe during pregnancy and breast feeding as well.

- Baseline test:** CBC, LFTs, BUN/Urea, Creatinine, Electrolytes, should be done before starting ATT. Stop/modify first line ATT when LFTs become raised, more than 3-times from normal value.

- Monitoring of Drugs therapy

- Monthly sputum samples for microscopy and culture

- Monitor drug side effects:** Renal retention parameters, ophthalmological check-up, ENT, and LFTs

- The American Thoracic Society recommends the initiation of therapy with first-line anti-TB for the treatment of TBM.

- First-line anti-TB agents = 'RIPE':** Rifampicin (R), Isoniazid (I), Pyrazinamide (P), Ethambutol (E) and/or Streptomycin (S).

Tab. Isoniazid (5-10mg/kg/day up to 300 mg/day)

Tab. Rifampicin (10-15mg/kg/day up to 600 mg/day)

Tab. Pyrazinamide (20-30mg/kg/day up to 2 gm/day)

Tab. Ethambutol (15-20mg/kg/day up to 1.2 gm/day).

For drug brand, strength & adverse effects see PTB – Pulmonology section

Active Disease

- Initiation phase:** 2 months of "RIPE" – Rifampicin (R), Isoniazid (I), Pyrazinamide (P), Ethambutol (E)

- Continuation phase:** 10 months of Isoniazid + Rifampin (2DRUGS)

- Adjunctive Corticosteroids therapy** have also been shown to decrease secondary complications with: Tab. Dexamethasone 5mg (Kanadex) Or Prednisolone 5mg (Deltacortril) tapered over 6–8 weeks in divided doses.
- Tapering dosage for 6 weeks** (week 1 = 60 mg, week 2 = 45 mg, week 3 = 30 mg; week 4 = 20 mg, week 5 = 10mg, week 6 = 5 mg)
- Follow physician order for supportive treatment:** Fever, headache $\uparrow$ ICP etc

ENCEPHALITIS

Definition: Encephalitis is defined as inflammation of the brain parenchyma associated with neurologic dysfunction, such as altered state of consciousness (ASOC), seizures, personality changes, cranial nerve palsies, speech problems, and motor and sensory deficits can be due to infectious (usually viral) or noninfectious (usually autoimmune) processes. An etiologic agent is only identified in around 50% of cases. In viral encephalitis the virus initially gains entry and replicates in local or regional tissue, such as the gastrointestinal tract, skin, urogenital system, or respiratory system. Subsequent dissemination to the central nervous system occurs by hematogenous routes (enterovirus, arboviruses, herpes simplex virus, HIV, mumps) or via retrograde axonal transport as with the herpes virus, the rabies virus, or variant scrapie-isoform prion proteins.

Clinical features

Prodromal phase

- » **Duration:** a few hours to days
- » **Nonspecific symptoms:** Fever, rash, headache, malaise, nausea & vomiting

Acute or subacute encephalopathy

- » **Focal neurological deficits** (primarily affects the medial temporal lobe)
Include: altered sense of smell & loss of vision, aphasia, hemianopia, hemiparesis, ataxia, brisk tendon reflexes, Babinski sign, cranial nerve deficits.
- » **Seizures** (focal or generalized)
- » **Altered mental status** (confusion, disorientation, lowered level of consciousness)
- » **Behavioral changes** (hypersexuality, hypomania, agitation)
- » **Meningism:** evidence of meningeal inflammation with headache, photophobia, and neck stiffness.
- » **Coma**

DIAGNOSTIC WORKUP

- » **CBC:** Often elevated WBC
- » **Peripheral blood smear:** detection of *Plasmodium falciparum* and Ehrlichia.
- » **BUN & Serum creatinine**
- » **Serum electrolytes:** Hyponatremia
- » **LFTs:** Deranged/elevated
- » **Blood glucose**
- » **Coagulation profile:**
- » **A lumbar puncture (LP)** for CSF analysis, CSF culture and CSF PCR. Do not delay empiric treatment if LP is delayed.
- » **Gold standard test:** CSF PCR (Most common HSV-1 and HSV-2) but may reveals other viruses or bacteria.
- » **Blood Culture:** Detection and confirmation of systemic bacterial infections and most arboviral infection.
- » **Sputum culture:** detection of TB
- » **Throat swab:** detection of viruses
- » **HIV serology/RNA test**
- » **Chest X-ray:** rule out TB, Sarcoidosis
- » **CT scan brain**



Stabilize patients using ABCD&E approach.

- » Check SpO₂ & Give high flow O₂ as appropriate.
- » Intubation with hyperventilation to a PaCO₂ of around 30
- » Elevated head of bed to 30°
- » Begin enteral feeding via nasoduodenal tube within 24 hours.
- » **Establish large-bore intravenous (IV) access.**
- » **Vitals monitoring:** Check BP, PR, RR, Temperature, SpO₂
- » **Obtained labs:** CBC, BUN, Creatinine, Electrolytes, LFTs, RBS & coagulation profile, CSF analysis, CSF culture and CSF PCR.
- » **All cases of suspected community-acquired viral encephalitis are started empirically on Inj. Acyclovir 500mg (Acyclovir, Aclovir) at dose 10 mg/kg x TDS (every 8 hourly) for 10-21 days.**
- » **Adjunct corticosteroids:** Inj. Methylprednisolone sodium succinate 1000mg (Solu-Medrol) x IV once daily for 3-5 days. Corticosteroids are often used in the treatment of acute viral encephalitis, although the efficacy of steroids has not been proven but ↓ raised ICP.
- » **Isotonic IV fluids:** Normal saline, R/L or D5%W are preferred to restore fluid balance and electrolyte levels.
- » **With fever:** Inj Paracetamol 1g/100ml (Provas, Paracet) x IV x TDS
- » **Gastroprotective:** Inj. Omeprazole 40mg (Ruling, Risek) x IV x OD
- » **With seizures:** Give Inj. Diazepam 10mg/2ml (Valium) x 10mg diluted in 8ml 0.9% NS OR D5%W x at dose 2mg up to 10mg x IV. For seizures prophylaxis: Inj. Levetiracetam 500mg/5ml (Lerace, Epilapsa) at dose 1-2g in 100ml 0.9% NS x IV over 15-20 minutes.
- » **Elevated intracranial hypertension (ICP):** Inj. Mannitol 250ml x IV x STAT then 100ml x BD/TDS (dose should be calculated according to the patients age and body weight)
- » Pass nasogastric tube and folly's catheter with attach urine bag
- » Monitor pupillary reflexes, Record GCS level & urine input/output.
- » **Shunting or surgical decompression (by craniectomy)** is indicated in some cases where medical management has failed to control elevated ICP, and for impending uncal herniation.

A lumbar puncture (LP) is always recommended as long as there is no contraindication, and 2 out of the following 4 symptoms are present: Fever, headaches, altered mental status of unknown etiology, meningismus (headache, photophobia, and neck stiffness). Contraindications to LP include mass effect causing potential herniation, coagulopathy, or open skin lesion at the site of entry.

- » LP should be delayed only under abnormal circumstances.
- » **Opening pressure:** usually normal in viral encephalitis but can be increased especially when meningoencephalitis is present.

ISCHEMIC STROKE (CEREBRAL INFARCTION/CVA)

For concise detail and outpatient treatment – see Ischemic stroke neurology section

Clinical features

- Sudden onset of focal neurologic deficits: vision loss or visual field defect, weakness, paresthesias, aphasia, ataxia (impaired coordination) and dysarthria
- Nonspecific symptoms: Loss of consciousness, nausea, vomiting, headache, vertigo/dizziness, and seizures.
- Common Stroke Symptoms by Vessel Territory
 - Anterior Circulation (Carotid Arteries): Weakness or numbness on one side of the face, arm, or leg, difficulty speaking or understanding speech, vision problems in one or both eyes, sudden severe headache.
 - Middle Cerebral Artery: Weakness or numbness on one side of the body, often affecting the face, arm, and leg, difficulty speaking or understanding speech, confusion, vision disturbances.
 - Posterior Circulation (Vertebrobasilar Arteries): Severe headache, dizziness or loss of balance, visual disturbances, difficulty swallowing, weakness or numbness on one side of the body, typically affecting the face and limbs.
 - Vertebral and Basilar Arteries: Difficulty speaking or understanding speech, loss of coordination and balance, visual disturbances, weakness, or numbness on one side of the body, often affecting the face and limbs.
 - Lacunar stroke: Limb and/or facial weakness (typically affects face, leg, & arm equally), speech difficulty, ataxia, paresthesias or numbness (typically affects face, leg, and arm equally).
- Symptoms suggesting a specific etiology:
 - Aortic dissection: chest pain, hypotension, dyspnea
 - Endocarditis: fever, heart murmur
 - ICH/SAH: sudden, severe headache

TREATMENT OF ISCHEMIC STROKE (CEREBRAL INFARCTION/CVA)

- Stabilize patients using ABCD&E approach.
- Establish large-bore intravenous (IV) access.
- Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂. Monitor pupillary reflexes and record GCS level.
- Urgent CT brain plain (without IV contrast).
- Consultation from Neuromedicine
- Dysphagia screening: Swallowing impairment is common in stroke and is associated with an increased risk of aspiration pneumonia and death. **Make patient NPO: until the risk of aspiration has been assessed.**
- Pass nasogastric tube and foley's catheter with attachment of urine bag and record urine input/output.
- Obtained labs: CBC, BUN, Creatinine, Electrolytes, LFTs, Blood glucose, coagulation profile, Troponin and other specific tests according patient's factors – see finding/interpretation in neurology section.
- IV fluids therapy: Ringer Lactate (R/L) & 0.9% NS x IV x BD/TDS to maintain hydration and hemodynamic stability. Recommended maintenance dose around 30-35 ml/kg/day for adults. Adjust fluid therapy based on individual patient factors such as age, comorbidities (e.g., heart failure, renal impairment), and hemodynamic status.
- Blood pressure: Systolic B.P between 150 and 220 mmHg, acute lowering of systolic B.P to a target of 140 mmHg with the goal of maintaining in the range of 130 to 150 mmHg is safe.
 - Inj. Labetalol 50mg/10ml x 20mg x IV once, then 20-80mg IV every 10 minutes, titrated as needed.
 - OR Inj. Hydralazine 20mg/1ml x diluted in 0.9% NS, loading dose 10-20mg over 5-10 min, then repeat after 20 min if desire BP is not achieved.
- Glycemic control: For secondary brain injury prevention
 - Hypoglycemia: Manage, if blood glucose is < 60 mg/dL.
 - Hyperglycemia: Manage and keep blood glucose levels between 140 to 180 mg/dL.
- Reperfusion therapy: Treatment decisions should be made by neurologist; consultation with neurologist.
- With seizures: Inj. Diazepam 10mg/2ml (Valium) diluted in 8ml 0.9% NS x at dose 5-10 mg (5-10ml) IV, may repeat if required. If unresponsive then treat it as status epilepticus (see status epilepticus). For seizures prophylaxis: Inj. Levetiracetam 500mg/5ml (Lerace, Epilapsa) at dose 1-2g in 100ml 0.9% NS x IV over 15-20 minutes.
- Maintaining normothermia and avoiding neurogenic fever "as associated with poor stroke outcome".
 - With fever/pain: Inj. Paracetamol 1g/100ml (Provas) x IV x TDS/SOS

- ✦ Venous thromboembolism (VTE) prophylaxis
- ✦ Anticoagulation: Treatment with anticoagulation should begin as soon as the diagnosis of cerebral venous sinus thrombosis (CVST) is confirmed. Specialist guidance should be sought to choose anticoagulation.
- ✦ Identify and treat any underlying complications such as aspiration pneumonia, UTI, DVT and pressure ulcer.
- ✦ Admit and monitoring of all patients in a HDU or ICU facility with 24-hour
- ✦ Follow-up in outpatient (OPD) – see discharge medications in neurology section

REPERFUSION THERAPY

- ✦ Consider Intravenous Thrombolytics: Treatment decisions should be made with consultation of neurologist for tailored treatment based on patient multiple factors.
 - » Agents: IV recombinant tissue plasminogen activator (tPA)
 - ✦ Inj. Alteplase at dose 0.9 mg/kg total dose IV, administer 10% of dose as a bolus over 1 minute, with the remaining 90% infused over 1 hour, maximum 90 mg total dose.
 - ✦ OR Inj. Tenecteplase at dose 0.25 mg/kg as a bolus, maximum per dose 25mg.
 - » Inclusion criteria
 - ✦ No evidence of stroke mimic or intracranial hemorrhage
 - ✦ Acute disabling neurological symptoms
 - ✦ The AHA/ASA recommend treating with alteplase:
 - (1) Within 3 hours of stroke symptom onset or patient last known well or at baseline state: medically eligible patients aged ≥ 18 years (equally recommended for patients aged < 80 and > 80 years); patients with severe stroke symptoms or mild but disabling stroke symptoms.
 - (2) Within 3.0 to 4.5 hours of stroke symptom onset or patient last known well for: patients aged ≤ 80 years; those without a history of both diabetes mellitus and stroke; those with a baseline National Institutes of Health Stroke Scale (NIHSS) score ≤ 25 ; those not taking any oral anticoagulants; those without imaging evidence of ischemic injury involving $> 1/3^{\text{rd}}$ of the middle cerebral artery territory.
 - (3) Unclear symptom onset > 4.5 hours from last known baseline state (e.g., wake-up stroke): MRI findings determine (patients with early ischemic changes) whether thrombolysis is indicated.
 - (4) Patients whose blood pressure can be lowered safely to $< 185/110$ mmHg with antihypertensive agents; those with initial glucose levels > 50 mg/dL.
 - » Complications of IV thrombolytic: Angioedema, intracranial hemorrhage, Extracranial hemorrhage
 - » Monitoring and additional measures after thrombolysis
 - ✦ Check blood pressure and neurological status frequently.
 - ✦ Avoid invasive procedures, if possible.
 - ✦ Obtain a follow-up CT brain (without IV contrast) or MRI brain 24 hours after thrombolysis, prior to starting anticoagulants or antiplatelet agents.

Contraindications to thrombolysis: Exclusion criteria for thrombolysis in acute ischemic stroke

Absolute Contraindications Mnemonic as SAMPLE STAGES.	Relative contraindications
» Seizures present at onset of stroke or nondisabling minor stroke (NIHSS < 5) » Acute bleeding diathesis: INR > 1.7, PT > 15 sec, or aPTT > 40 sec. ↓ platelet count: $< 100,000/\text{mm}^3$, & anticoagulation agent » Myocardial infarction (MI) in the past 3 months. » Presence of intraaxial intracranial neoplasm » Large areas of marked hypodensity on CT » Elevated uncontrolled hypertension (BP $> 185/110$ mm Hg) » Major Surgery in the past 14 days » TIA (mild or rapid improvement of symptoms) within 6 months. » Acute intracranial (or SAH), Active internal bleeding, Acute infective endocarditis, Acute aortic arch dissection » GI or genitourinary bleeding in the past 21 days » Glucose $\downarrow < 50$ mg/dL or Elevated glucose: > 400 mg/dL. » Stroke or head trauma within the last 3 months. » Recent Surgery intracranial or intraspinal (≤ 3 months ago)	» Very severe stroke (NIHSS > 25) > 3 hours after event » Acute pericarditis » Intracranial conditions that may increase bleeding risk » Recent major surgery or trauma (not including head) (< 14 days ago) » History of bleeding diathesis or coagulopathy » Current malignancy/cancer » History of cerebral microbleeding » GI or genitourinary bleeding > 21 days » Known left atrial or ventricular thrombus. » Pregnancy or early postpartum period (< 14 days after delivery) » Recent arterial puncture (< 7 days ago)

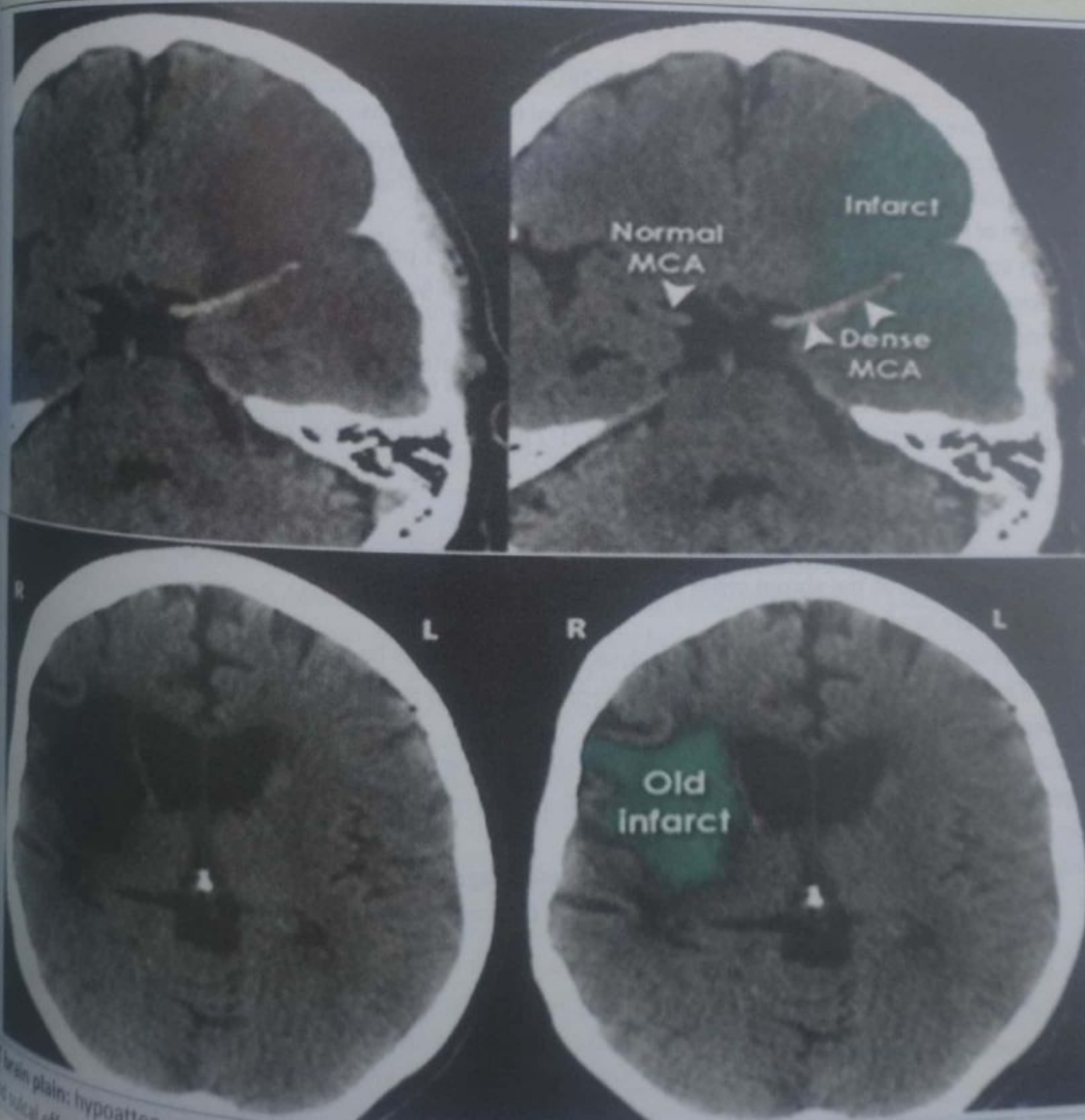
MECHANICAL THROMBECTOMY

Description: physical retrieval or aspiration of the occluding thrombus via the femoral artery using a stent retriever and/or an aspiration catheter.

Inclusion criteria

- Age ≥ 18 years
- Acute large artery occlusion causing a stroke: e.g., proximal artery occlusion in anterior cerebral circulation (M1) or occlusion of the internal carotid artery.
- Disabling stroke symptoms (NIHSS ≥ 6)
- Limited affected area on CT (Alberta Stroke Program Early CT Score ≥ 6)
- Previously independent in ADLs (prestroke modified Rankin scale (mRS) ≤ 1)
- Patients with symptom onset within the past 6 hours or selected patients with symptom onset between 6 and 24 hours ago

Patients who are eligible for tPA should receive thrombolysis immediately, while mechanical thrombectomy is being considered. If indicated, mechanical thrombectomy should be performed without delay to assess the response to thrombolysis.



Brain plain: hypoattenuation (darkness) of the brain parenchyma; loss of gray matter-white matter differentiation, sulcal effacement; hyperdensity in an artery is indicative of a possible thrombosis

INTRACEREBRAL HEMORRHAGE (ICH)/INTRAPARENCHYMAL HEMORRHAGE

- Definition: Hemorrhagic stroke is defined as cerebral hemorrhage is due to rupture of a cerebrospinal artery, resulting in intraparenchymal hemorrhage, subarachnoid hemorrhage (SAH), and intraventricular hemorrhage.
- Intracerebral hemorrhage (ICH) or Intraparenchymal hemorrhage is defined as bleeding within the brain parenchyma most commonly caused by systemic hypertension. ICH is further sub-divided into primary and secondary etiology. Primary spontaneous ICH is defined as hemorrhage in the absence of vascular malformations or associated diseases. Secondary ICH is from an identifiable vascular malformation or as a complication of other medical or neurologic diseases that either impair coagulation or promote vascular rupture.
- Location of ICH: It is helpful sub-divided ICH by location because etiologies and prognosis vary by site: 1. Lobar: occurs in the cortex or subcortical white matter of the cerebral hemispheres. 2. Deep hemispheric: occurs in the supratentorial deep gray matter structures, most commonly the putamen, globus pallidus of basal ganglia and thalamic nuclei. 3. Brain stem: occurs mostly in the pons. 3. Cerebellar: occurs mostly in the dentate nucleus.
- Strong risk factors: Hypertension, Advance age (> 65 years of age), Male sex, Ethnicity (Asian, Black, Hispanic), Family history of cerebrovascular disease (ICH, CVA), hemophilia, cerebral amyloid angiopathy (recurrent lobar hemorrhagic stroke in older adults), sickle cell diseases, autosomal dominant mutations in the COL4A1 gene, hereditary hemorrhagic telangiectasia, autosomal dominant mutations in the KRIT1 CCM2 or PDCD10 genes, anticoagulation, Recreational drug use (IV drugs, cocaine, heroin, amphetamines, and ecstasy), Vascular malformations, Moyamoya disease, pregnancy. Weak risk factors: smoking, NSAIDs, diabetes, heavy alcohol use, cerebral vasculitis, thrombocytopenia, leukemia, long sleep duration & poor sleep quality, obstructive sleep apnea.

STROKE SCALES

- The NIH Stroke Scale is a rapid physical assessment tool for stroke signs.
- The Intracerebral Hemorrhage (ICH) Score is the most widely used severity-of-illness grading scale for prognosticating outcomes early after onset of intracerebral hemorrhage.
- Elements of the ICH score include:
 - » ICH Volume: If the volume of the hemorrhage is $> 30 \text{ cm}^3$, = 1 point.
 - » Glasgow Coma Score (GCS): GCS of 3-4 = 2 points, or GCS of 5-12 = 1 point.
 - » Intraventricular hemorrhage: If present = 1 point.
 - » Infratentorial ICH location: If the hemorrhage is in the infratentorial region, = 1 point.
 - » Age: If the patient is older than 80 years, = 1 point.
- Interpretation of ICH Score: 0 points = Lowest risk, 1-2 points = Intermediate risk, 3-5 points = Highest risk

CLINICAL FEATURES

- Generally, presents as the abrupt onset of a focal neurologic deficit.
- Sudden, severe headache
- Focal neurological deficits: weakness or paralysis on one side of the body, slurred speech, and visual disturbances.
- ALOC: Confusion, lethargy, or coma may occur depending on the severity of the hemorrhage.
- Nausea and vomiting
- Seizures: Especially if the hemorrhage irritates the surrounding brain tissue.
- Signs of increased intracranial pressure (ICP): Papilledema (swelling of the optic disc), bradycardia, and hypertension.
- Other features depending on the location of the hemorrhage may manifest, such as:
 - » Hemiparesis or hemiplegia (weakness or paralysis on one side of the body)
 - » Sensory deficits
 - » Visual disturbances
 - » Difficulty with speech or swallowing
 - » Balance and coordination problems

DIAGNOSTIC WORKUP

- Initial test: CT brain without IV contrast** – Shows hyperdense area. It's a crucial test to differentiate hemorrhagic from ischemic stroke. CT may also be used as a follow-up exam to evaluate expansion and worsening mass effect.
- GCS Score:** score for prognosis after early onset of intracerebral hemorrhage
- Complete blood count (CBC):** Usually normal or may show thrombocytopenia or anemia.
- Blood glucose level:** may exclude hypoglycemia or hyperglycemia.
- BUN and creatinine:** may exclude acute kidney injury/renal failure. Usually normal.
- Serum electrolytes:** may exclude electrolyte disturbance. Usually normal.
- Liver function tests (LFTs):** to assess liver dysfunction. May be deranged.
- Coagulation profile (PT, APTT & INR):** usually normal.
- Additional test for evaluating etiology:**
- **Other tests if indicated:** Fasting lipid profile (8-12 hours fasting), HbA1c, Serum TSH
 - **Urine tests:** Urinalysis, urine culture, urine pregnancy test and urine toxicology
 - **Chest x-ray:** if a lung disease is suspected. normal; or cardiomegaly, aortic dissection, pneumonia
 - **ECG:** may exclude ischemia or arrhythmia.
 - **Cardiac enzyme:** Serum troponin – if signs of myocardial ischemia. may exclude myocardial infarction.
 - **Lumbar puncture** (if SAH suspected and CT brain negative for blood).
 - **EEG,** if seizure is suspected.
 - **CT angiography (CTA) and venography:** Aneurysm, AV malformation, or cerebral sinus/venous thrombosis
 - **MR angiography and venography:** Aneurysm, AV malformation, or cerebral sinus/venous thrombosis
 - **Conventional (invasive) angiography:** Aneurysm or AVM
 - **MRI brain:** Aneurysm, arteriovenous malformation, tumor, cerebral sinus/venous thrombosis, cerebral infarction
 - **MRI brain with DWI & GRE:** Acute hemorrhage appears hypointense (dark) in gradient-echo

TREATMENT OF INTRACEREBRAL HEMORRHAGE (ICH)/HEMORRHAGIC STROKE

- **Stabilize patients using ABCD&E approach.**
- **Establish large-bore intravenous (IV) access.**
- **Vitals monitoring:** Check BP, PR, RR, Temperature, SpO₂. Monitor pupillary reflexes and record GCS level.
- **Anticoagulation reversal:** Stop all anticoagulants and antiplatelet agents. Consider administering reversal agents as soon as possible to patients with an INR > 1.4 to reduce the risk of hematoma expansion. Treatment involves administering blood products such as fresh frozen plasma (FFP), prothrombin complex concentrate (PCC), and specific clotting factors to replenish depleted coagulation factors and restore normal clotting function.
- **Urgent CT brain plain (without IV contrast).**
- **Consultation from Neuromedicine**
- **Dysphagia screening:** Swallowing impairment is common in stroke and is associated with an increased risk of aspiration pneumonia and death. **Make patient NPO: until the risk of aspiration has been assessed.**
- **Pass nasogastric tube and foley's catheter** with attachment of urine bag and record urine input/output.
- **Obtain investigations:** CBC, BUN, Creatinine, Electrolytes, LFTs, Blood glucose, coagulation profile, ECG, Troponin, Chest-x-ray and other specific tests according patient's factors.
- **IV fluids therapy:** Ringer lactate (R/L) x 1L and 0.9% N.S x 1L x IV x BD/TDS. Recommended maintenance fluids around 30-35 ml/kg/day for adults. Adjust fluid therapy based on individual patient factors such as age, comorbidities (e.g., heart failure, renal impairment), and hemodynamic status.
- **Blood pressure:** Systolic B.P between 150 and 220 mmHg, acute lowering of systolic B.P to a target of 140 mmHg with the goal of maintaining in the range of 130 to 150 mmHg is safe. **Avoid hypotension (MAP < 65 mm Hg).**
- **Inj. Labetalol 50mg/10ml x 20mg x IV once,** then 20-80mg IV every 10 minutes, titrated as needed.
- **OR Inj. Hydralazine 20mg/1ml x diluted in 09 ml 0.9% NS,** loading dose 10-20mg over 5-10 min, then repeat after 20 min if desire BP is not achieved. (for more detail see hypertensive emergency – mention above)
- **Alternative antihypertensive medications:** ACE inhibitors (Captopril) or ARBs (Losartan) and Furosemide
- **Hypertensive control:** For secondary brain injury prevention
- **Hypoglycemia:** Manage, if blood glucose is < 60 mg/dL.
- **Hyperglycemia:** Manage and keep blood glucose levels between 140 to 180 mg/dL

- ☛ With seizures: Inj. Diazepam 10mg/2ml (Valium) diluted in 8ml 0.9% NS x at dose 5-10 mg (5-10ml) IV, may repeat if required. If unresponsive then treat it as status epilepticus (see status epilepticus). For seizures prophylaxis: Inj. Levetiracetam 500mg/5ml (Lerace, Epilapsa) at dose 1-2g in 100ml 0.9% NS x IV over 15-20 minutes.
- ☛ Maintaining normothermia and avoiding neurogenic fever "as associated with poor stroke outcome".
- ☛ With fever/pain: Inj. Paracetamol 1g/100ml (Provas) x IV x TDS/SOS or PO Tab. Panadol 500-1000mg x TDS/QID
- ☛ DVT prophylaxis: initiate intermittent pneumatic compression (Compression stockings) of the legs as patients are at increased risk of VTE. **N.B. Oral/IV anticoagulants for VTE prophylaxis are contraindicated seek specialist adv.**
- ☛ Elevated intracranial hypertension (ICP): Treat by elevating head-end of the bed to 30°, starting hypertonic saline or mannitol, and hyperventilating the patient.
Mannitol infusion 20%/500ml (=100 grams) x Initial dose: 0.25-1.5 g/kg IV as a single dose (for 70 kg patients' weight, the initial dose = 87.5 - 525 ml) over 30 to 60 minutes, with effects usually seen within 5 to 10 minutes and lasting up to about 6 hours. Maintenance Dose: 0.25-0.5 g/kg IV every 6 hours or as needed.
 - ☛ Dosage should be adjusted according to the patient's age, body weight, and renal function.
 - ☛ Need for external ventriculostomy catheter, intracranial pressure (ICP) monitor or surgical intervention.
 - ☛ Monitor closely for signs of hematoma expansion; discontinue Mannitol if observed.
- ☛ Monitor for Hematoma/hemorrhage expansion:
 - » Perform regular neurological examinations.
 - » Consider:
 - ☛ Early CT angiography (CTA): within 3 hours of assessment (to assess for hematoma expansion).
 - ☛ CT brain without contrast: 24 hours after presentation to determine the final size of the hematoma.
 - ☛ Transcranial duplex ultrasonography
- ☛ Identify and treat any underlying complications such as aspiration pneumonia, UTI, DVT and pressure ulcer.
- ☛ Admit and monitoring of all patients in a HDU or ICU facility with 24-hour.
- ☛ Neurosurgical consultation for surgical intervention
- ☛ Follow-up in outpatient (OPD) – see discharge medications in neurology section

SURGICAL MANAGEMENT OPTIONS FOR ICH

- ☛ Hematoma evacuation, via standard craniotomy or minimally invasive stereotactic aspiration is recommended for infratentorial hemorrhages with large hematomas, declining neurological status, hydrocephalus, or signs of brain herniation. For supratentorial hemorrhages, consider evacuation with declining or initial GCS scores of 10-13. Decompressive craniotomy, alone or with evacuation, is considered for supratentorial hemorrhages with refractory elevated ICP, large hematomas causing significant midline shift, or GCS score ≤ 8 .
- ☛ Additional Intervention: External ventricular drain (EVD) placement is recommended for draining excess cerebrospinal fluid and reducing intracranial pressure. Endoscopic surgery: Use of an endoscope to access and remove the hematoma through small incisions, minimizing damage to surrounding brain tissue



Hypertensive hemorrhages (Charcot Bouchard microaneurysm) most often occur in putamen and globus pallidus of basal ganglia (lenticulostriate vessels (A)), followed by internal capsule, thalamus, pons, and cerebellum (B). Source: RX-2024 & IMPP-24

(C) Hyperdense area (Red arrow), effacement of the occipital horn of the left LV, and midline shift (dashed line & blue arrow). Right occipital horn (Yellow arrow)

(D) Hyperdense area (Yellow arrows) involving the right thalamus & the right internal capsule. Intraventricular hemorrhage (Red arrows). Mass effect has caused a slight midline shift.

ANAPHYLAXIS

Clinical features

- Swelling of mucous membranes
- Flushing, erythema
- Urticaria, pruritus
- Swelling of the eyelids
- Angioedema
- Nasal congestion
- Sneezing
- Respiratory
 - Cough, hoarseness, Chest tightness.
 - Dyspnea (due to bronchospasm)
 - Tachypnea, Stridor, wheezing
 - Hypoxia, cyanosis
- Gastrointestinal: Nausea, vomiting (esp. in food allergies), Abdominal pain, diarrhea
- Cardiovascular
 - Hypotension
 - Tachycardia
 - Weak peripheral pulses
- Signs of end-organ dysfunction
 - Altered mental status, Syncope
 - Decreased urine output, Anuria
 - Skin changes: e.g., mottling
 - Low temperature
 - Delayed capillary refill (> 2 sec)
 - Ischemic chest pain



TREATMENT OF ANAPHYLAXIS

- Stabilize patient using ABCD&E approach
- Stop offending medication, remove inciting allergens.
- Give high flow O₂ as needed, Aim to keep SpO₂ 94-98%
- Establish intravenous (IV) access
- Vitals monitoring: BP, PR, RR, Temperature and check SpO₂
- Obtain labs: CBC, serum tryptase level, serum IgE level, serum basophil activation test (BAT) and allergy skin prick test
- Inj. Adrenalin 1mg/ml (1:1,000) at dose 0.3 – 0.5mg (or 0.01ml/kg to maximum 0.5ml) into the anterolateral thigh, repeat after 5-15 minutes if no improvement. Inj. Adrenalin for anaphylaxis should always be given IM in a concentration of 1:1,000 (as opposed to the 1:10,000 solution used in cardiac arrest). Avoid injecting the 1:1,000 solution into a vein can lead to cardiac arrhythmia/arrest.
- Persistent respiratory symptoms: Salbutamol (Ventolin solution) at dose 2.5 to 5mg in 3mL NS is nebulized every 20 minutes for 3 doses, then every 1-4 hours when required
- IV fluid: 0.9% normal saline 1 – 2L x IV Bolus (if Hypotension – Inj. Haemaccel 500ml x IV x stat then SOS)
- Give Inj. Pheniramine maleate 25mg/2ml (Avil) x IV x STAT
- Corticosteroids: Inj. Methylprednisolone sodium succinate 500mg/vial (Solu-Medrol) at dose 1-2mg/kg/day x IV.



BENZODIAZEPINES POISONING

Clinical Features

- Lethargy
- Drowsiness, Somnolence
- Confusion
- Impaired coordination
- Slurred speech, Ataxia
- Respiratory depression
- Hypotension (mild)
- Hypotonia and hyporeflexia
- Coma (in severe cases)
- Nystagmus, which typically accompanies alcohol and phenytoin overdose, is absent in the case of benzodiazepine overdose.



TREATMENT OF BENZODIAZEPINES POISONING

- Stabilize patients using ABCD&E approach.
- Establish large-bore intravenous (IV) access.
- Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂
- Pass Nasogastric tube and foley's catheter.
- Obtained labs: CBC, BUN, Creatinine, electrolytes, LFTs, RBS, PT, INR, ABGs and urine toxicology screening.
- IV Crystalloid fluid: Inj R/L & 0.9% N/S 1L x IV x BD/TDS
- IV Antibiotics: Inj. Co-Amoxiclav 1.2g (Augmentin) x IV x BD OR Inj. Ceftriaxone 2g (Oxidil, Rocephin) x diluted in 100ml 0.9%NS x IV, OD
- Gastric protective: Inj Omeprazole 40mg (Risek, Ruling) x IV x OD
- Inj. Haemaccel 500ml x IV x SOS (hypotension/shock)
- ANTI-DOTE: Inj Flumazenil 1mg/10ml: The recommended initial dose of Flumazenil is 0.3 mg IV, If the required level of consciousness is not obtained within 60 sec, a further dose of 0.1 mg can be injected and repeated at 60-sec intervals, up to a total dose of 2 mg or until the patient awakes. If drowsiness recurs, an intravenous infusion of 0.1 – 0.4 mg/h may be useful. Routine use of flumazenil for benzodiazepine overdose is not recommended, should be used in caution because it causes seizure.
- Monitor pupillary reflexes, GCS level & Cardiac monitoring.
- Observe patient for 12-24hours

APPROACH TO THE POISONED OR OVERDOSE PATIENTS

1. Initial ER management: Stabilize the patient with primary survey using modified ABCD&E approach
 - A. Airway: Anticipate airway loss due to impending obstruction or depressed mental status and consider prophylactic airway protection.
 - Assessment
 - » Airway obstruction or injury
 - Caustic agents
 - Toxic inhalation injuries
 - Toxic seizures
 - » Increased Risk of aspiration or bronchial obstruction
 - Loss of airway protective reflexes
 - Excessive vomiting or hematemesis
 - Management
 - » Airway obstruction
 - Caustic or inhalation injury: high risk of difficult airway
 - Call for help for anesthesia/anesthetic team
 - Perform intubation as soon as possible.
 - Uncontrollable seizures: Abort convulsive activity & perform Rapid sequence intubation (RSI)
 - » Loss of airway protection
 - Begin basic airway maneuvers.
 - Consider early intubation for patients expected to deteriorate with:
 - Severely depressed mental status or coma
 - ↑ Risk of aspiration due to excessive vomiting
 - ↑ Risk of status epilepticus
 - » Transient airway compromise (Isolated GHB toxicity, post-ictal period): Consider basic airway maneuvers alone with close airway monitoring.
 - B. Breathing: Consider the effect of the toxin on the respiratory drive.
 - Assessment
 - » Decrease respiratory rate (RR)
 - Opioids
 - Sedative-hypnotics
 - » Increase respiratory rate (RR) or Kussmaul respirations
 - Stimulants toxicity: Amphetamines, cocaine
 - Acute salicylate (aspirin) ingestion
 - Compensation for toxin-induced metabolic acidosis: e.g., toxic alcohols
 - Aspiration pneumonia
 - Management
 - » In all patients
 - Start SpO₂ monitoring and provide oxygen therapy as needed.
 - Begin bag valve-mask ventilation if signs of respiratory failure.
 - Consider arterial blood gas (ABG) analysis (or VBG) to screen for acid-base disorders.
 - » Carbon monoxide toxicity (CO toxicity) – An intoxication with the gas carbon monoxide (CO)
 - Administer high-flow 100% O₂.
 - Interpret pulse oximetry with caution in patients with CO toxicity
 - » Opioid-induced respiratory depression or respiratory arrest: Give naloxone for opioid overdose.
 - » Consider intubation and mechanical ventilation for:
 - Respiratory failure unresponsive to antidotes (e.g., naloxone)
 - Significant acidemia and evidence of respiratory muscle fatigue
- N.B. In mechanically ventilated patients with severe metabolic acidosis, optimize tidal volume and respiratory rate to match the patient's respiratory compensation.

C. Circulation: Check ECG to identify and treat cardiotoxic substance exposure.

➤ Assessment

- » Hypotension: due to opioids, digoxin, antihypertensives
- » Hypertension
 - Central neurological complication (e.g., cocaine-associated stroke)
 - Sympathomimetics
- » Toxin-induced rhythm and conduction abnormalities
 - Bradycardia: due to beta blockers, calcium channel blockers (CCBs)
 - Narrow complex tachycardia: vasodilators, sympathomimetics
 - QRS widening and wide complex tachycardia: due to sodium channel blockers drugs such as TCAs (Nortriptyline, amitriptyline) and antiarrhythmics drugs

➤ Management

- » All patients
 - Start continuous cardiac monitoring and also consider hemodynamic monitoring for patients with shock.
 - Establish intravenous (IV) access.
 - Provide immediate hemodynamic support as needed: IV fluid resuscitation
- » Toxin-induced bradycardia
 - Give high-dose atropine for muscarinic cholinergic symptoms
 - Consider consultation from cardiology ward for temporary cardiac pacing.
- » Toxin-induced tachyarrhythmias
 - Consider benzodiazepines (IV Diazepam, Midazolam) if stimulants are suspected.
 - Administer 8.4% sodium bicarbonate for severe sodium channel blocker toxicity (TCA toxicity)
- » Toxin-induced hypotension: typically requires treatment with adrenergic vasopressors
 - Negative inotropes: Epinephrine is preferred (see general drug dilution)
 - Peripheral vasodilators: Norepinephrine is preferred (see general drug dilution)
- » Cardiovascular drug toxicity: often associated with refractory arrhythmias and shock
 - Examples: beta-blocker toxicity, CCB toxicity, cardiac glycoside toxicity
 - Consider toxin-specific antidotes in addition to immediate hemodynamic support, such as:
 - High-dose insulin therapy (with regular insulin)
 - IV calcium: calcium chloride OR calcium gluconate
 - Digoxin-immune fab
 - Consider extra-corporeal life support (ECMO) for refractory life-threatening cases.

D. Disability: Treat alterations in glucose metabolism and/or toxic seizures.

➤ Assessment

- » Evaluation of mental status via – Glasgow coma scale (GCS).
- » Check Pupillary response – examine closely for mydriasis and miosis.
- » Hypoglycemia causes include: insulin and oral hypoglycemics
- » Toxic seizures causes include: Insulin and oral hypoglycemics, antidepressants, Sympathomimetics, Lead, Lithium, Isoniazid.
- » Withdrawal seizures: from alcohol, benzodiazepines.

➤ Management

- » Altered mental status:
 - **DO NOT ADMINISTER A "COMA COCKTAIL" EMPIRICALLY, RATHER CONSIDER EACH ANTIDOTE ON AN INDIVIDUAL BASIS.**
 - Consider IV naloxone for opioid-induced coma (Opioid overdose explained in detail below)
 - Give D50%W (or D25%W) for hypoglycemia.
 - Give IV thiamine (Inj. Neurobion) if risk factors present for Wernicke encephalopathy (e.g., malnourishment, alcohol use disorder)
 - Reevaluate mental status (GCS) frequently.
- » Toxic seizures: see management of status epilepticus – section emergency medicine.
 - First-line: Benzodiazepines (Diazepam, Lorazepam, Midazolam)
 - Second line: Barbiturates (Phenobarbitone, Thiopental)
 - Consider Neurology consultation

N.B. Do not treat toxic seizures with phenytoin, which can worsen the cardiotoxic effects of certain drugs (tricyclic antidepressants, theophylline, and cocaine) and is ineffective in seizures caused by withdrawal or isoniazid.

» **Cyanide toxicity:**

- Give Hydroxycobalamin
- OR Sodium nitrite followed immediately by sodium thiosulfate

E. **Exposure:** Look for clues for the underlying toxin and perform surface decontamination.

➤ **Assessment**

» **Skin abnormalities – via physical examination**

- » Evidence of chemical exposure
- » Transdermal medication patches
- » **Track marks:** small holes in the skin and are often the clearest drug addiction signs due to frequent injection of addictive drugs

» **Evaluation for Hyperthermia:**

- **Serotonin syndrome:** due to SSRIs, SNRIs, TCAs, Triptan
- **Neuroleptic malignant syndrome:** due to antipsychotics, Metoclopramide, Carbamazepine, Promethazine, Venlafaxine
- **Malignant hyperthermia:** due to Volatile anesthetics (halothane), Succinylcholine
- **Anticholinergic toxicity:** due to Belladonna poisoning, anticholinergic drugs such as Atropine, Benztropine, Trihexyphenidyl, TCAs, Antipsychotics, Promethazine, and Dimenhydrinate.

➤ **Management**

» **Chemical or radiological exposures:** providers trained in decontamination should:

- Remove all of the patient's clothing
- Immediately irrigate the body
- Avoid irrigation with water if the patient was exposed to an alkali metal

» **Hyperthermia**

- Discontinue causative agent
- Begin active cooling, e.g., mist and fan.

2. Identify classic toxidromes as well as for signs and symptoms of specific poisonings (see below)

3. Consider the need for decontamination &/or specific antidotes are required during or after stabilization.

- **Body surface decontamination:** should be considered in any case of known or suspected exposure to chemical, biological, radiologic, or nuclear (CBRN) hazards. It involves the removal of any residual toxin from the patient's skin and mucous membranes
- **Or time-sensitive Gastrointestinal (GI) decontamination:** removal of a toxin from the body before it is absorbed by the gastrointestinal tract
 - » **Single-dose activated charcoal:** oral or nasogastric (NG) tube administration of activated charcoal
 - » OR **Gastric lavage:** Administration of warm saline or water via a large-bore orogastric tube, followed by aspiration of the fluid, in order to remove pills and pill debris.
 - » OR **Whole bowel irrigation:** oral or NG tube administration of large volumes of an osmotically balanced solution (e.g., polyethylene glycol electrolyte solution) to flush the bowel
- **OR Enhanced elimination techniques:** Refers to the removal of a toxin from the body after it has been absorbed by the GI tract under supervision of poison control team.
 - » **Multidose activated charcoal (MDAC)**
 - » OR **Urine alkalinization:** IV infusion of sodium bicarbonate promotes renal elimination by trapping by basic ions in the urine.
 - » OR **Extracorporeal elimination techniques:** Consult nephrology unit before use. Hemodialysis, continuous renal replacement therapy, or hemoperfusion remove toxins via an extracorporeal process.

4. Identify and treat life-threatening complications:

- **With Cardiac arrhythmia –** consider cardiological consultation.
- **With Seizures –** see treatment of status epilepticus.

5. Once the patient has been stabilized, continue the toxicological risk assessment.

6. Consider reassurance and discharge with instructions for patients with unintentional nontoxic exposures

ORGANOPHOSPHATE POISONING

Diagnostic approach

History Assessment:

History: Obtain a detailed history of exposure, including the type of organophosphate (e.g., insecticides, nerve agents), route of exposure (inhalation, ingestion, dermal), and duration of exposure.

Symptoms: Look for the classic signs of cholinergic excess, which can be remembered using the acronym "SLUDGE" (Salivation, Lacrimation, Urination, Diarrhea, Gastrointestinal distress, Emesis) and "DUMBELS" (Diarrhea, Urination, Miosis, Bronchorrhea/Bronchospasm, Emesis, Lacrimation, Salivation).

Physical Examination:

Muscarinic effects: Pinpoint pupils (miosis), excessive salivation, sweating, lacrimation, bronchospasm, bronchorrhea, bradycardia, hypotension, abdominal cramps, diarrhea, urinary incontinence.

Nicotinic effects: Muscle fasciculations, weakness, paralysis, tachycardia, hypertension.

Central nervous system effects: Anxiety, confusion, seizures, coma.

Diagnostic Tests:

Cholinesterase Activity: Measure plasma cholinesterase (butyrylcholinesterase) and red blood cell cholinesterase (acetylcholinesterase) levels, which are typically reduced in organophosphate poisoning.

Other tests: CBC, Urea, Electrolytes, LFTs, RBSs, ABGs, and ECG to assess for complications.

TREATMENT OF ORGANOPHOSPHATE POISONING

Stabilize patients using ABCD&E approach.

Make patient Nil per oral (NPO)

Pass nasogastric (NG) tube & foley's catheter with attach urine bag.

Decontamination:

Remove Contaminated Clothing: Immediately remove contaminated clothing and thoroughly wash the skin with soap and water to prevent further absorption.

Ocular Exposure: Irrigate eyes with saline or water for at least 10-15 minutes.

Gastric Lavage: Consider if the patient presents within 1 hour of ingestion, and if the airway is protected.

Establish large-bore intravenous (IV) access.

Vitals monitoring: Check BP, PR, RR, Temperature, SpO2

Check SpO2 & Give high flow O2 as appropriate.

Start IV fluids: 0.9% NS or R/L 1000ml x IV x STAT.

Obtain labs: CBC, Urea, Electrolytes, Creatinine, LFTs, RBS, PT INR, ABGs and anticholinesterase level.

ANTIDOTES:

Inj. Atropine

Initial dose: 2-4 mg IV bolus/STAT

Repeat every 5-15 minutes until bronchorrhea and bronchospasm are controlled, and adequate oxygenation is achieved. Large cumulative doses may be required.

ALTERNATIVE PROTOCOL BY LOCAL HOSPITAL:

Inj. Atropine 2-4mg x IV x STAT dose.

Then 1mg/ml for 2 days every 15 minutes.

Then 1mg/ml for 1 day every 30 minutes.

Then 1mg/ml for 1 day every 1 hour.

Then 1mg/ml for 1 day every 2 hours.

Then 1mg/ml for 1 day every 4 hours.

OR Pralidoxime (2-PAM): Given the high side effect profile and current clinical practice, pralidoxime use is often limited. WHO dose: 30mg/kg x IV x Stat over 20-30minutes then 8mg/kg/hour. continues infusion until recovery of patients. OR Inj. Pralidoxime 2g in 100ml 0.9% NS x slow IV x STAT, then followed by 500mg per hour for 7 days.

Gastroprotective: Inj. Omeprazole 40mg (Ruling, Omezol) x IV x OD

Prophylactic antibiotics: Inj. Ceftriaxone 2g (Oxidil, Rocephin), diluted in 100 ml 0.9% NS x IV x OD

OPIOID OVERDOSE (OPIOID TOXICITY)

△ Opioid overdose

C/C:

Classic triad of Opioid toxidrome:

1. Altered mental status: CNS depression, euphoria
 2. Bilateral pinpoint pupils (miosis)
 3. Opioid-induced respiratory depression
- ⚠ N.B. The absence of miosis does not rule out opioid intoxication.

(OIRD)

Opioid-induced respiratory depression

- » Respiratory rate ↓ and/or apnea
- » Tidal volume ↓
- » Disordered control of breathing
- » Signs of respiratory distress
- » Signs of hypercapnic respiratory failure
→ ↑ EtCO₂ (End-tidal CO₂) = Partial pressure of carbon dioxide (in mm Hg) present in the air at the end of expiration.
- » Can progress to respiratory arrest

⚠ N.B. OIRD is the most common cause of death from opioid overdose & is treated with naloxone for opioid overdose.

Other features include:

- » Respiratory: Pulmonary edema (Non-cardiogenic)
- » CNS: Myoclonic jerks, seizures and Diminished or absent gag reflex
- » GIT: Constipation & ↓ bowel sounds, Nausea and vomiting
- » CVS: Bradycardia, Hypotension
- » Other: Hypothermia, Pruritus, flushing

DIAGNOSTIC & CLINICAL APPROACH

• Opioid overdose is a clinical diagnosis based on suggestive clinical features (opioid toxidrome) and a compatible history of substance exposure.

• Begin empiric management of opioid overdose as soon as it is clinically suspected; do not wait for confirmatory diagnostic tests

Examine for signs of:

- » Skin and soft tissue infections.
- » Compartment syndrome.
- » Adherent Fentanyl ^{Sandoz} skin patches
- » Pulmonary edema
- » Cardiac murmur

Rx

- Stabilize patients using ABCD&E approach.
- Establish large-bore intravenous (IV) access.
- Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂ (Check SpO₂ & Give high flow O₂ as appropriate)
- Start IV fluids: 0.9% NS or R/L 1000ml x IV x STAT.
- Obtain labs: CBC, BUN/urea, creatinine, and electrolytes, LFTs, Blood glucose, CPK, urine toxicology, s/acetaminophen and ABGs.
- Administer naloxone for opioid overdose in patients with opioid-induced respiratory depression.
 - ⚠ Inj. Naloxone 0.4–2mg x IV once, titrate further dosing to clinical response → respiratory rate, tidal volume, EtCO₂, and other signs of respiratory distress or respiratory failure.
 - ⚠ No improvement: Repeat the dose every 2–3 min as needed. Consider increasing the dose on each repeat administration if there is no response. Repeat doses can range widely; follow local protocols and tailor to the individual clinical response. After ≥ 10 mg of naloxone, reconsider the diagnosis and evaluate for other causes of respiratory depression.
 - ⚠ Initial improvement with recurrent OIRD: Start continuous infusion at ⅓ the naloxone dose that initially reversed OIRD. Titrate the infusion based on clinical response.
 - ⚠ Precipitated opioid withdrawal: Not give additional naloxone.
- With vomiting – consider ONE of the following anti-emetics:
 - ⚠ Inj. Metoclopramide 10mg/2ml (Metaclo) x IV x TDS
 - ⚠ OR Inj. Dimenhydrinate 50mg/ml (Gravinate) x IV x TDS
 - ⚠ OR Inj. Ondansetron 8mg/4ml (Onset, Onseron) x diluted in 50 to 100 ml of 0.9% NS OR D5%W, IV over 15 minutes.
- With seizures: Give Inj Diazepam (Valium) 10mg/2ml x diluted in 8ml 0.9% N/S x 2mg up to 10mg x IV.
- Consider IV thiamine: Inj Neurobion 2–4 ml in IV fluids.
- Determine if the overdose was intentional, a suicide attempt.
- Observe patient for 6–8 hours, once the patient is medically stable, he should be referred for a psychiatric assessment.

DIAGNOSTIC WORKUP

• Usually done to check for other existing conditions, complications.

Laboratory test

- » Bedside blood glucose to rule out severe hypoglycemia.
- » Serum acetaminophen and salicylate levels.
- » BUN/Urea, creatinine and electrolytes to assess for AKI.
- » Creatine phosphokinase (CPK) to assess for rhabdomyolysis.
- » Urine toxicology, if there is concern for multidrug toxicity.

Radiological test:

- » Chest x-ray (CXR): To assess chest pathology, pulmonary edema.
- » ECG: Assess for life-threatening ECG findings, e.g., QTc ≥ 500 ms, cardiac arrhythmias and ectopy, and/or ischemic ECG changes

Naloxone infusion: Inj. Naloxone 0.4mg/ml, Dilution 5 ampule of naloxone (= 2mg) – diluted in 500ml solution of D5%W or 0.9% normal saline (NS). Final strength after dilution in 500ml = 4 mcg (Usual dose is 100mcg–400mcg (25ml–100 ml) per hour can increase up to 800 mcg (200 ml) per hour). Continuous infusion doses of naloxone in mcg & ml – see below (100mcg = 25ml, 200mcg = 50ml, 400mcg = 100ml, 500mcg = 125ml, 600mcg = 150ml, 700mcg = 175ml, 800mcg = 200ml)

PARACETAMOL (ACETAMINOPHEN) OVERDOSE

Minimum toxic dose of paracetamol: 7.5 g/day in adults. – Maximum daily dose is 4 g (adults).
Drug induced hepatitis – Leading cause of acute hepatic failure.

Pathophysiology: Massive hepatic centrilobular necrosis (elevated LFTs)/fulminant liver failure

ANTIDOTE = N-acetylcysteine: Treat overdose with N-acetylcysteine → replenishes glutathione

DIAGNOSTIC APPROACH

Clinical Assessment

- History: Obtain a detailed history of Paracetamol (acetaminophen) intake, including amount, timing, and form (e.g., tablets, liquid).
- Symptoms: Initial symptoms may include nausea, vomiting, abdominal pain, and confusion. Severe cases can lead to liver failure, jaundice, coagulopathy, and encephalopathy.

Diagnostic workup:

- Serum Acetaminophen levels: at least 4 hours post-ingestion to assess toxicity and guide treatment. Levels should be plotted on the Rumack-Matthew nomogram to determine risk.
- Liver Function Tests (LFTs): Check for elevated liver enzymes (AST, ALT, ALP) and bilirubin levels.
- Coagulation Profile: Assess PT/INR for potential liver dysfunction.
- Electrolytes, Urea, Creatinine: Monitor electrolytes, renal function, and metabolic status.
- Abdominal Ultrasound: May be used to evaluate liver size and presence of fluid or other abnormalities.



TREATMENT OF PARACETAMOL (ACETAMINOPHEN) OVERDOSE

- Stabilize patients using ABCD&E approach.
- Make patient Nil per oral (NPO)
- Establish large-bore intravenous (IV) access.
- Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂ (Check SpO₂ & Give high flow O₂ as appropriate)
- Obtained labs: CBC, Urea, Electrolytes, Creatinine, LFTs, RBS, PT INR, acetaminophen level and ABGs.
- Gastrointestinal Decontamination
 - Activated Charcoal: Administer if the patient presents within 1-2 hours of ingestion and is alert and able to protect their airway. Dosage is typically 1g/kg.
 - Lavage: Gastric lavage is generally not recommended unless the patient presents within 1 hour of ingestion and is unconscious or has a compromised airway.
- Antidote Administration: N-Acetylcysteine (NAC): Administer NAC as soon as possible, ideally within 8-10 hours of ingestion. NAC is effective in preventing or minimizing liver damage if administered early.

The treatment regimen typically includes:

- Oral N-Acetylcysteine 200mg sachets (Muculator) at loading dose of 140 mg/kg followed by 70 mg/kg every 4 hours for a total of 17 doses. Dilute the solution to about 5% with water, juice, or soda. If vomiting interferes with oral N-acetylcysteine administration, consider giving the antidote intravenously.
- IV infusion of N-Acetylcysteine 200mg/ml (Mucomix)
 - Loading dose: 150 mg/kg diluted in 200ml 5%DW OR 0.45% NS, administered over 60 minutes
 - Dose 2: 50 mg/kg in 500ml 5%DW OR 0.45% NS, administered over 4 hours
 - Dose 3: 100 mg/kg in 1000ml 5%DW OR 0.45% NS administered over 16 hours
 - Dose 3: 100 mg/kg in 1000ml x IV x BD/TDS, to maintain hydration and support blood pressure.
- Start IV fluids: 0.9% NS or R/L 1000ml x IV x BD/TDS, to maintain hydration and support blood pressure.
- Electrolyte Management: Correct any imbalances and monitor renal function.
- Gastroprotective: Inj. Omeprazole 40mg (Risek, Ruling) diluted in 100ml 0.9% NS x IV x OD
- Prophylactic antibiotics: Inj. Ceftriaxone 2g (Oxidil, Rocephin) diluted in 100ml 0.9% NS x IV x OD
- With vomiting – consider ONE of the following anti-emetics:
 - Inj. Metoclopramide 10mg/2ml (Metacloclon) x IV x TDS
 - OR Inj. Dimenhhydrinate 50mg/ml (Gravinate) x IV x TDS
 - OR Inj. Ondansetron 8mg/4ml (Onset, Onseron) x diluted in 50 to 100 ml of 0.9% NS OR D5%W, IV over 15 min.
- Management of Complications
 - Treatment of Liver Failure: Monitor for signs of acute liver failure and manage accordingly. Consider referral to a liver specialist. Liver transplant in severe cases
 - Hepatic Encephalopathy: Provide supportive care and monitor neurological status.

AMPHETAMINES OVERDOSE

- ☛ **Substance:** Amphetamines – are a class of sympathomimetic agents → naturally occurring substances such as cathinone (khat), from the plant *Catha edulis*, and ephedrine (ephedra) from the plant *Ephedra sinica*.
 - » **Classic drugs:** Methamphetamine, dextroamphetamine, and methylphenidate; these substances can be synthesized illicitly from pseudoephedrine and ephedrine, which are available as over-the-counter (OTC) cold medicines
 - » **Substituted amphetamine drugs:** MDMA (3,4-methylenedioxymethamphetamine), Methyldiethanolamine (MDEA)
- ☛ **Street names:** speed (methylphenidate-like substances); uppers; ice meth crystal meth (methamphetamines); Molly (MDMA)
- ☛ **Mechanism of action:** increased release and inhibited reuptake of adrenaline, norepinephrine, serotonin, and dopamine → sympathetic stimulation and hallucinogenic effects

CLINICAL FEATURES

- ☛ **Presenting symptoms:** anxiety, tremulousness, tachycardia, hypertension, diaphoresis, dilated pupils, agitation, muscular hyperactivity, and psychosis. Muscle hyperactivity may lead to metabolic acidosis and rhabdomyolysis.
- ☛ **Autonomic symptoms:** Diarrhea, diaphoresis, hypertension, tachycardia, palpitation, chest pain, cardiac arrhythmias, hyperthermia, increased libido, mydriasis, decreased appetite, weight loss, grinding teeth (can lead to broken teeth), itching (can lead to excoriations)
- ☛ **Neuropsychiatric symptoms:** Altered mental status (severe agitation, confusion, hallucinations, coma), euphoria, paranoia, psychosis, sleep disorders, prolonged wakefulness, hyperalertness, megalomania, disorganized thinking, delusional parasitosis (the delusion that the body is infested with parasites or bugs)
- ☛ **Abnormal neuromuscular activity:** Hyperreflexia, myoclonus, hypertonia (rhabdomyolysis), tremors, seizures
- ☛ **Signs of serotonin toxicity:** Agitation, diaphoresis, fever $>100^{\circ}\text{F}$ (38°C), tremor, hyperreflexia, hypertonicity and spontaneous, induced, or ocular clonus.
- ☛ Toxicity from amphetamines cannot be readily distinguished clinically from cocaine toxicity, but the management in both cases is essentially the same. The prevalence of ischemic chest pain and stroke in cocaine intoxication is higher. Urine drug screen will differentiate cocaine from amphetamines.

DIAGNOSTIC WORKUP

- ☛ **Laboratory tests:**
 - » **Blood glucose:** $>60\text{ mg/dL}$
 - » **Serum electrolytes:** normal or sodium $<130\text{ mEq/L}$
 - » **Serum creatinine & BUN/urea:** creatinine $>1.5\text{ mg/dL}$; BUN $>20\text{ mg/dL}$
 - » **LFTs:** abnormal (AST $>30\text{ U/L}$; ALT $>40\text{ U/L}$, gamma-GT $>30\text{ U/L}$)
 - » **Coagulation profile:** aPTT & INR – normal or prolonged
 - » **Serum D-dimer:** maybe elevated
 - » **Serum creatine kinase (CK):** normal or greatly elevated (e.g., peak $>30,000\text{ U/L}$)
 - » **Serum troponin:** normal or elevated (warranted in patients with chest pain consistent with ischemia, may be detected 4 to 8 hours after myocardial infarction and persist for up to 10 days).
 - » **ABGs:** pH <7.35 , metabolic acidosis
 - » **Urinalysis:** Dark yellow, specific gravity >1.020 ; dipstick normal or may be positive for blood (rhabdomyolysis)
 - » **Urine drug screening:** Amphetamines/Cocaine are usually detectable in urine for at least 48 hours.
- ☛ **Radiological tests:**
 - » **Electrocardiography (ECG):** may show tachycardia, may show arrhythmias, ischemic changes.
 - » **Chest x-ray (CXR):** may show pulmonary edema, pneumothorax, pneumomediastinum.
 - » **CT scan brain:** may be indicated (rarely intracranial hemorrhage, SAH, cerebral edema)



TREATMENT OF AMPHETAMINES OVERDOSE

Follow the standard protocol for poisoned patients (see above “Approach to the poisoned patients”)

- ☛ **Stabilize patients using ABCD&E approach.**
- ☛ **Establish large-bore intravenous (IV) access.**
- ☛ **Decontamination:**
 - » If the patient presents within 1 hour of drug ingestion and is cooperative, activated charcoal 50g is given orally as a single dose, may repeat at 4–6-hour intervals
 - » If intoxication is mild, the patient may be best managed by monitoring and observation in a quiet environment, with supportive measures (intravenous fluids, cooling) as needed.

- Pass nasogastric (NG) tube, Folly's catheter with attachment of urine bag
- Monitor pupillary reflexes, record GCS level, record urine input and output.
- Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂ (Check SpO₂ & Give high flow O₂ as appropriate)
- Obtained labs: Send initial 1st order laboratory tests: CBC, BUN/urea, electrolytes, creatinine, LFTs, blood glucose, PT APTT & INR, d-dimer, creatine kinase (CK), troponin-i, ABGs, urinalysis and urine drug screening
- Radiology: obtain chest x-ray (CXR), ECG (arrhythmia, ACS), and CT scan brain to identify the cause of seizures.
- IV fluid therapy: Ringer lactate, Normal saline – The average patient may require 3-5L of IV fluids for volume depletion or rhabdomyolysis in the first few hours of admission.
- Patient with agitation:
 - With mild to moderate agitation: Tab. Diazepam 10mg (Valium) or Tab. Lorazepam 2mg (Ativan) or Tab. Olanzapine 5mg (Olanzia) x per orally single dose, may repeat if required
 - With severe agitation (Richmond Agitation-Sedation Scale +3 to 4)
 - ⊕ Diazepam 10/2ml at dose 5-10 mg IV as a single dose, may repeat if necessary
 - ⊕ OR Midazolam 5mg/5ml at dose 5mg IV/IM as a single dose, may repeat if required
 - ⊕ If unresponsive to benzodiazepines – consider antipsychotics: Inj. haloperidol 5mg (Serenace) 2.5 mg to 5 mg IM/IV as a single dose or Inj. Droperidol 5mg/2ml 2.5mg to 5 mg IM/IV as a single dose
- Patient with hyperthermia: defervescence and muscle paralysis
 - with hyperthermia >100°F (>38°C) but <103°F (<39.5°C)
 - ⊕ Active cooling is generally instituted when body temperature exceeds 100°F (38°C). The simplest method to accomplish rapid cooling in any setting is the application of tepid mist and use of a fan for conductive, evaporative, and convective heat dissipation. Additional measures include cooling blankets and ice packs. Care should be taken to monitor for hyponatremia.
 - ⊕ Benzodiazepines (Diazepam, Midazolam) are given to relax muscles: Inj. Diazepam 10mg/2ml (Valium) at dose 5-10 mg IM/IV as a single dose, may repeat if required OR Inj. Midazolam 5mg/5ml (Dormicum) x at dose 5mg IV/IM as a single dose, may repeat if required
 - with hyperthermia >103°F (>39.5°C)
 - ⊕ Indicates severe, potentially life-threatening toxicity and mandates immediate cooling (e.g., cooled intravenous fluids, sponge baths, ice packs) and sedation.
 - ⊕ In general this is best done in the intensive care unit (ICU) with paralysis and ventilation.
 - ⊕ Paralysis may need to be prolonged to prevent re-emergence of drug-induced hyperthermia and is usually accomplished with a **non-depolarizing neuromuscular blocker** with moderate duration of action such as Pancuronium or Rocuronium or Vecuronium should be given under local specialist consultant protocol for guidance on dose. Patients must be intubated before initiation of paralysis.
- Patient with seizures: Inj. Diazepam 10mg/2ml (Valium) diluted in 8ml 0.9% NS x at dose 5-10 mg (5-10ml) IV, may repeat if required. If unresponsive than treat as status epilepticus (explained above)
- Patient with hypertension: see Hypertensive emergency (explained above)
 - ⊕ Inj. Labetalol 50mg/10ml at dose 10-20 mg IV every 10 minutes until desired blood pressure is achieved, maximum 300 mg/total dose
 - ⊕ OR Inj. Nitroglycerin at dose 5-200 mcg/min x IV (see General drug dilution for infusion & dilution)
 - ⊕ OR Inj. Nitroprusside at dose 0.3 mcg/kg/min IV initially, titrate to achieve desired blood pressure, maximum 10 mcg/kg/min. (see General drug dilution for infusion & dilution)
- Patient with hypotension: Trendelenburg position and vasopressors
 - ⊕ Hypotension is a late-stage phenomenon that may occur if the patient is severely dehydrated or has depleted catecholamines. An immediate temporizing effect may be obtained by placing the patient into the Trendelenburg position. Copious intravenous fluid administration is warranted.
 - ⊕ IV Administration of vasopressors: (see General drug dilution)
 - ⊕ Dopamine at dose 1-50 mcg/kg/min IV
 - ⊕ Norepinephrine at dose 2-12 mcg/min IV
- Patient with cardiac dysrhythmia: consultation with cardiology department
- If metabolic acidosis: Sodium bicarbonate may be required to correct a severe metabolic acidosis.
- Consider gastroprotective: Inj. Omeprazole 40mg/vial (Risek, Ruling) x IV x OD
- Consider antibiotics if evidence of secondary infection: Inj. Ceftriaxone 2g (Oxidil Titan, Rocephin) x IV x OD

COCAINE OVERDOSE

- ☛ **Substance:** cocaine, crack cocaine (free base form of cocaine) – Naturally occurring alkaloid found in *E. coca* plant
- ☛ **Street names:** coke, blow
- ☛ **Forms of preparation:** powder or rocks that are insufflated, smoked, or injected intravenously.
- ☛ **Mechanism of action:**
 - » Inhibition of dopamine, serotonin, and norepinephrine uptake → increased dopamine in the synaptic cleft of the endogenous reward system
 - » Inhibition of Na⁺ channels causes local anesthetic action by blocking nerve action potential transmission.

CLINICAL FEATURES

- ☛ Snorting can cause damage to the nasal vessels and result in nosebleeds.
- ☛ Local vasoconstriction may cause ischemic necrosis, resulting in a perforated nasal septum.
- ☛ **Cocaine intoxication**
 - » Euphoria, arousal, increased vigilance, impaired judgment, alertness, grandiosity
 - » Anxiety, irritability, mood swings, psychotic symptoms (e.g., paranoia, hallucinations)
 - » Sweating, tachycardia, hypertension, chest pain/angina
 - » **Mydriasis**
 - ↳ Can be used in the diagnosis of Horner syndrome.
 - ↳ Instillation of cocaine into the eyes will produce mydriasis in the eye with intact sympathetic innervation, whereas the denervated pupil will not (or only barely) dilate.
 - » **Tachyarrhythmia**
 - » Can result in sudden cardiac death
 - » Paranoia, tactile, acoustic, and optic hallucinations
 - » Malignant hyperthermia

DIAGNOSTIC WORKUP

- ☛ **Laboratory tests:**
 - » **Blood glucose:** > 60 mg/dL
 - » **Serum electrolytes:** normal or sodium <130 mEq/L
 - » **Serum creatinine & BUN/urea:** creatinine >1.5 mg/dL; BUN >20 mg/dL
 - » **LFTs:** abnormal (AST >30 U/L; ALT >40 U/L, gamma-GT >30 U/L)
 - » **Coagulation profile:** aPTT & INR – normal or prolonged
 - » **Serum D-dimer:** maybe elevated
 - » **Serum creatine kinase (CK):** normal or greatly elevated (e.g., peak >30,000 U/L)
 - » **Serum troponin:** normal or elevated (warranted in patients with chest pain consistent with ischemia, may be detected 4 to 8 hours after myocardial infarction and persist for up to 10 days).
 - » **ABGs:** pH <7.35, metabolic acidosis
 - » **Urinalysis:** Dark yellow, specific gravity >1.020; dipstick normal or may be positive for blood (rhabdomyolysis)
 - » **Urine drug screening:** Amphetamines/Cocaine are usually detectable in urine for at least 48 hours.
- ☛ **Radiological tests:**
 - » **Electrocardiography (ECG):** may show tachycardia, may show arrhythmias, ischemic changes.
 - » **Chest x-ray (CXR):** may show pulmonary edema, pneumothorax, pneumomediastinum.
 - » **CT scan brain:** may be indicated (rarely intracranial hemorrhage, SAH, cerebral edema)



TREATMENT OF COCAINE OVERDOSE

Follow the standard protocol for poisoned patients (see above "Approach to the poisoned patients")

- ☛ **Stabilize patients using ABCD&E approach.**
- ☛ **Establish large-bore intravenous (IV) access.**
- ☛ **Decontamination:**
 - » If the patient presents within 1 hour of drug ingestion and is cooperative, activated charcoal 50g is given orally as a single dose, may repeat at 4-6 hour intervals
 - » If intoxication is mild, the patient may be best managed by monitoring and observation in a quiet environment, with supportive measures (intravenous fluids, cooling) as needed.

- Pass nasogastric (NG) tube, Folly's catheter with attachment of urine bag
- Monitor pupillary reflexes, record GCS level, record urine input and output.
- Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂ (Check SpO₂ & Give high flow O₂ as appropriate)
- Obtained labs: Send initial 1st order laboratory tests: CBC, BUN/urea, electrolytes, creatinine, LFTs, blood glucose, PT APTT & INR, d-dimer, creatine kinase (CK), troponin-i, ABGs, urinalysis and urine drug screening
- Radiology: obtain chest x-ray (CXR), ECG (arrhythmia, ACS), and CT scan brain to identify the cause of seizures.
- IV fluid therapy: Ringer lactate, Normal saline – The average patient may require 3-5L of IV fluids for volume depletion or rhabdomyolysis in the first few hours of admission.
- Patient with agitation:
 - » With mild to moderate agitation: Tab. Diazepam 10mg (Valium) or Tab. Lorazepam 2mg (Ativan) or Tab. Olanzapine 5mg (Olanzia) x per orally single dose, may repeat if required
 - » With severe agitation (Richmond Agitation-Sedation Scale +3 to 4)
 - ↳ Diazepam 10/2ml at dose 5-10 mg IV as a single dose, may repeat if necessary
 - ↳ OR Midazolam 5mg/5ml at dose 5mg IV/IM as a single dose, may repeat if required
 - ↳ If unresponsive to benzodiazepines – consider antipsychotics: Inj. haloperidol 5mg (Serenace) 2.5 mg to 5 mg IM/IV as a single dose or Inj. Droperidol 5mg/2ml 2.5mg to 5 mg IM/IV as a single dose
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 - » with hyperthermia >100°F (>38°C) but <103°F (<39.5°C)
 - ↳ Active cooling is generally instituted when body temperature exceeds 100°F (38°C). The simplest method to accomplish rapid cooling in any setting is the application of tepid mist and use of a fan for conductive, evaporative, and convective heat dissipation. Additional measures include cooling blankets and ice packs. Care should be taken to monitor for hyponatremia.
 - ↳ Benzodiazepines (Diazepam, Midazolam) are given to relax muscles: Inj. Diazepam 10mg/2ml (Valium) at dose 5-10 mg IM/IV as a single dose, may repeat if required OR Inj. Midazolam 5mg/5ml (Dormicum) x at dose 5mg IV/IM as a single dose, may repeat if required
 - » with hyperthermia >103°F (>39.5°C)
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 - ↳ In general this is best done in the intensive care unit (ICU) with paralysis and ventilation.
 - ↳ Paralysis may need to be prolonged to prevent re-emergence of drug-induced hyperthermia and is usually accomplished with a **non-depolarizing neuromuscular blocker** with moderate duration of action such as Pancuronium or Rocuronium or Vecuronium should be given under local specialist consultant protocol for guidance on dose. Patients must be intubated before initiation of paralysis.
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- Patient with hypertension: see Hypertensive emergency (explained above)
 - » Inj. Labetalol 50mg/10ml at dose 10-20 mg IV every 10 minutes until desired blood pressure is achieved, maximum 300 mg/total dose
 - » OR Inj. Nitroglycerin at dose 5-200 mcg/min x IV (see General drug dilution for infusion & dilution)
 - » OR Inj. Nitroprusside at dose 0.3 mcg/kg/min IV initially, titrate to achieve desired blood pressure, maximum 10 mcg/kg/min. (see General drug dilution for infusion & dilution)
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 - » Hypotension is a late-stage phenomenon that may occur if the patient is severely dehydrated or has depleted catecholamines. An immediate temporizing effect may be obtained by placing the patient into the Trendelenburg position. Copious intravenous fluid administration is warranted.
 - » IV Administration of vasopressors: (see General drug dilution)
 - ↳ Dopamine at dose 1-50 mcg/kg/min IV
 - ↳ Norepinephrine at dose 2-12 mcg/min IV
- Patient with cardiac dysrhythmia: consultation with cardiology department
- If metabolic acidosis: Sodium bicarbonate may be required to correct a severe metabolic acidosis.
- Consider gastroprotective: Inj. Omeprazole 40mg/vial (Risek, Ruling) x IV x OD
- Consider antibiotics if evidence of secondary infection: Inj. Ceftriaxone 2g (Oxidil Titan, Rocephin) x IV x OD

CORROSIVE POISONS (ACIDS/CAUSTIC INGESTION)

EXAMPLES OF CAUSTICS/ACIDS:

ACIDS:

- » Sulphuric Acid: Car Batteries
- » Nitric Acid: Metal Cleaners
- » Hydrochloric Acid and Acetic Acid
- » Phenol and Boric Acid
- » Hydrofluoric and Oxalic Acid (Rust Removers)

ALKALIS

- » Ammonia: House-Hold cleaners & laundry detergents
- » Bleach (Disinfectant)
- » Sodium Hydroxide: Drain Cleaners

WHY NOT TO DO:

- » **GASTRIC LAVAGE:** Risk of perforation (Immediate lavage within 1hrs. after large volume of ingestion is maybe beneficial)
- » **EMESIS:** Leads to new exposure and risk of aspiration.
- » **NEUTRILIZATION:** Leads to heat production more injury.
- » **ACTIVATED CHARCOAL:** Obscures endoscopic view.

PPI & SUCRALFATE INTERACTIONS

- » PPI (Omeprazole, esomeprazole) and sucralfate can interact, potentially reducing the effectiveness of omeprazole.
- » To minimize this interaction, it's recommended to take sucralfate at least 2 hours before or after omeprazole.

Rx

- » Stabilize patients using ABCD&E approach.
- » **NO GASTRIC LAVAGE** (contraindicated – May induced retching and vomiting which can cause compound injury), avoid induced vomiting.
- » **IMMEDIATE FIRSTAID:**
 - » Rinse the mouth with water to remove any remaining substance.
 - » **Immediate Dilution:** Encourage the patient to drink water, milk, or eats ice-cream to dilute the corrosive substance and reduce its contact with the GI tract.
 - » **Syp. Aluminium Hydroxide** (Mucain, Gaviscon) 60-80ml STAT then repeat 40-60ml x every 15-20min.
- » Establish large-bore intravenous (IV) access.
- » Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂.
- » Start IV fluids 0.9% NS or R/L 1000ml x IV x STAT.
- » Obtained labs: CBC, Blood sugar, BUN/Urea, Electrolytes, Creatinine, LFTs PT&INR, & ABGs.
- » Gastric protective: Inj. Omeprazole 40mg (Omezol, Ruling) OR Inj. Esomeprazole 40mg (Esso, Nexum) x diluted in 100 ml 0.9% NS x IV x OD.
- » IV Antibiotics: Inj. Co-Amoxiclave 1.2g/vial (Augmentin) x IV x BD OR Inj. Ceftriaxone 1-2g (Oxidil, Rocephin) x diluted in 100ml 0.9% NS x IV, STAT.
- » **With pain/analgesia:**
 - » Inj. Paracetamol 1g/100ml (Provas, Paracet) x IV x TDS/SOS
 - » OR Inj. Ketorolac 30mg/ml (Toradol) in 4ml 0.9% N/S x IV
 - » OR Inj. Tramadol 100mg/2ml (Tramol) + Inj. Dimenhydrinate 50mg/ml (Gravinate) dilute in 100ml 0.9% NS.
 - » OR Inj. Nalbuphine 10mg/ml (Kinz) + Inj. Dimenhydrinate 50mg/ml (Gravinate) dilute in 100ml 0.9% NS.
- » **With laryngeal edema:** Inj. Hydrocortisone 100mg-250mg x IV x TDS/BD; Alternative Inj Dexamethasone (Decadron 4mg/1ml)
- » **REASSURE & FOLLOW-UP CARE:**
 - » Patients may require long-term follow-up to monitor for potential complications (scarring or narrowing of the esophagus or stomach).
 - » Counseling and support may be provided for patients and their families regarding prevention of future ingestions and coping with potential long-term effects.
- » **DISCHARGE MEDICATION:**
 - » Tab. Esomeprazole 40mg (Esso) x OD
 - » Syp. Sucralfate (Ulsanic) x 2 (10ml) teaspoonful x BD
 - » Take sucralfate at least 2 hours before or after taking omeprazole to allow for adequate absorption of both drugs.
 - » Tab. Moxifloxacin 400mg (Avelox, Moxiget) x OD

KEROSENE POISONING

Clinical features

- Mostly patient is asymptomatic with history of exposure.
- Symptoms soon after ingestion → typically progress to respiratory failure.
- Characteristic odour**
- Respiratory system:** symptoms usually occur within 30 minutes of exposure. Immediate signs are coughing, choking, gagging. Signs of pulmonary injury are dyspnea, cyanosis wheezing, rales, nasal flaring, grunting and fever. Fever >48 hours indicate bacterial superinfection.
- CVS:** Dysrhythmias, hypotension, and shock.
- CNS:** Headache, LOC, dizziness, ataxia, seizures, tremors and coma
- GI:** Burning sensation, nausea, vomiting, hematemesis & abdominal pain
- Skin and mucous membrane:** mucosal irritation and chemical burns

Diagnostic workup

- Petroleum distillate odor may emanate from the mouth/cloths
- Arterial Blood Gas (ABG) will show hypoxemia and hypercarbia.
- Bedside pulse oximetry:** ↓ SpO₂ (Hypoxia)
- CBC** may reveal raised WBCs
- Chest X-ray:** may be normal up to 6-12 hours post aspiration following which pneumonitis may be seen.
- ECG** may reveal arrhythmia if the poisoning is severe.
- Observe patient in ER for 6-8 hours
- Do not induce vomiting
- Do not attempt gastric lavage
- Risk of aspiration outweighs any benefit from removal of substance
- There is no role for steroids
- Pneumatocoles usually resolve spontaneously

Rx

- Stabilize patients using ABCD&E approach.
- Contaminations: NO GASTRIC LAVAGE (contraindicated)**
 - Cutaneous decontamination: Remove contaminated clothing. Irrigate affected skin, eyes and hair. Wash with soap and water.
 - Gastric decontamination is not recommended. The risk of aspiration due to emesis and gastric lavage outweigh the benefits. Activated charcoal does not bind well to hydrocarbons while it increases the risk of spontaneous vomiting and further aspiration.
- Establish large-bore intravenous (IV) access.
- Make patient Nil per oral (NPO).
- Vitals monitoring:** Check BP, PR, RR, Temperature, SpO₂ (Check SpO₂ & Give high flow O₂ as appropriate)
- Start IV fluids:** 0.9% NS or R/L 1000ml x IV x STAT
- Obtained labs:** CBC, Blood sugar, BUN/Urea, Electrolytes, Creatinine, LFTs PT&INR, & ABGs.
- IV Antibiotics:** Inj. Co-Amoxiclave 1.2g/vial (Augmentin) x IV x BD OR Inj. Ceftriaxone 1-2g (Oxidil, Rocephin) x diluted in 100ml 0.9% NS x IV x STAT.
- Indication of antibiotics:** Fever more than 48 hours, increasing infiltrates on chest x-ray, Sputum/tracheal aspirate yield culture positive.
- With vomiting – consider ONE of the following anti-emetics:**
 - Inj. Metoclopramide 10mg/2ml (Metacloclon) x IV x TDS
 - OR Inj. Dimenhydrinate 50mg/ml (Gravinate) x IV x TDS
 - OR Inj. Ondansetron 8mg/4ml (Onset, Onseron) x diluted in 50 to 100 ml of 0.9% NS OR D5%W, IV over 15 minutes.
- With seizures/fits:** Give Inj. Diazepam 10mg/2ml (Valium) x diluted in 8ml 0.9% NS or D5%W x IV 2mg upto 10mg over 5 minutes. **If recurrent seizures:** Inj. Levetiracetam (Lerace, Epilapsa) at dose 500mg – 1g in 100ml 0.9% NS x IV slow over 15-20 minutes (**Dosage:** 10mg/kg).
- Treatment is mainly supportive, NO SPECIFIC ANTIDOTE



PARAPHENYLENE DIAMINE (PPD) POISONING (KALA-PATHAR)

PPD is a coal-tar derivative, used as a hair dye agent after mixing with hydrogen peroxide and ammonia which on oxidation produces Bondrowski's base having allergenic, mutagenic and highly toxic properties. It is also used for tattooing due to its darkening effect when it is mixed with henna (*Lawsonia Alba*). They are salty, but not bitter in taste which makes it easy to be used as a poison. Lethal dose = 6-10 grams.

CLINICAL FEATURES

- » **Head, neck & Respiratory:**
 - ↳ Oral erythema, Swelling of lips, tongue, neck and eyelids.
 - ↳ Pain in throat
 - ↳ Breathing difficulty
 - ↳ Hoarseness of voice
 - ↳ Stridor (high-pitched sound while breathing)
 - ↳ Dysphonia (difficulty speaking)
 - ↳ Cervicofacial edema (swelling of face and neck)
 - ↳ Dysphagia (difficulty swallowing)
 - ↳ Difficulty in opening mouth
- » **Musculoskeletal:** Myalgia/rigidity
- » **Urinary:** (Dark urine)
 - ↳ Chocolate-brown-colored urine
 - ↳ Rhabdomyolysis
 - ↳ Oliguria/anuria (decreased or absent urine output)
 - ↳ Acute renal failure (ARF)
 - ↳ Hyperkalemia (elevated potassium levels)
- » **Hepatic:** Hepatitis
- » **Cardiovascular:**
 - ↳ Hemodynamic shock
 - ↳ Sinus bradycardia: ↓ heart rate
 - ↳ Sinus tachycardia: ↑ heart rate

DIAGNOSTIC WORKUP

- » **CBC:** Leukocytosis (↑ WBCs) or evidence of hemolysis.
- » **Liver Function Tests (LFTs):** Assess for liver damage, which can occur in severe cases.
- » **BUN & Creatinine:** Shows ARF
- » **Creatinine Kinase (CK):** ↑ levels may indicate muscle damage.
- » **ABGs:** acidosis or hypoxemia.
- » **Urinalysis:** signs of kidney damage or myoglobinuria.
- » **ECG:** for cardiac complications
- » **Chest X-ray:** for respiratory issues

TREATMENT OF PPD POISONING

- » **Stabilize patients using ABCD&E approach.**
 - ↳ Check SpO₂ & Give high flow O₂ as appropriate.
 - ↳ Endotracheal intubation, tracheostomy, and assisted ventilation were crucial and lifesaving measures.
 - ↳ Perform urgent tracheostomy if laryngeal edema.
- » **Establish large-bore intravenous (IV) access.**
- » **Vitals monitoring:** Check BP, PR, RR, Temperature, SpO₂
- » **Pass Nasogastric tube and Foley's catheter.**
- » **Gastric lavage:** Perform gastric lavage with 2 grams of activated charcoal every 6 hours, useful within 1 hour after ingestion.
- » **Make patient Nil per oral (NPO).**
- » **Start IV fluids:** R/L, 0.9% N/S & Inj D5%W x IV
- » **Obtain labs:** CBC, BUN, creatinine, electrolytes, LFTs, RBS, LDH, CPK, PT, APTT&INR, phosphorus, bicarbonate level & ABGs on daily basis
- » **Forced diuresis** with diuretics + IV fluid 5-6L is used to enhance the excretion of toxins via urine.
 - ↳ Give Inj. Furosemide 40mg/2ml (Lasix) 20mg every 8 hours.
 - ↳ Give Inj. Mannitol 250ml (If the patient is still oliguric).
- » **Gastric protective:** Inj. Inj. Omeprazole 40mg (Omezol, Risek) x IV x OD
- » **IV Antibiotics:** Inj. Co-Amoxiclav 1.2g (Augmentin) x IV x BD OR Inj. Ceftriaxone 2g (Oxidil, Rocephin) x diluted in 100ml 0.9%NS x IV, OD
- » **With laryngeal edema:** Give IV Inj. Methylprednisolone at dose 1mg/kg/day for 5 days OR Inj. Hydrocortisone sodium (Solu-Cortef) 250mg x IV STAT than 100mg for 7 days x TDS PLUS Inj. Pheniramine maleate 50mg/2ml (Avil) x TDS, for 3-5days for Cervicofacial edema.
- » **IV Sodium bicarbonate** to be given to prevent myoglobin precipitation in kidney at average dosage 1 ampule (22.5 mEq) in 500ml D5%W
- » **If develops Hyperkalemia:** Give inj. calcium gluconate 10%/10ml 8 hourly and salbutamol (Ventoline) nebulization every 3 hours.
OR Give Cocktail for hyperkalemia (See Hyperkalemia ER treatment)
- » **Cardiac Support:** If hypotension persists despite adequate fluid resuscitation, give Inj. Dopamine infusion at the rate of 6-8mcg/kg body weight per minute in order to maintain systolic BP above 90 mmHg.
- » **With ARF:** Plasma pheresis or Dialysis is required for patients.
- » **Treatment is mainly supportive and NO SPECIFIC ANTIDOTE**
- » **Skin Examination:** Assess skin involvement for burns, blisters, or discoloration.
- » **Consultation:** Seek toxicology advice for treatment guidance and early referral to nephrology, pulmonology, and otolaryngology departments is advised for comprehensive management
- » **Serial Monitoring:** Continuously assess clinical status and response to treatment.

WHEAT PILL POISONING (RICE PILL POISONING)

Definition: "Wheat pill" or Aluminum Phosphide poisoning, or rice pill is widely used as a **rodenticide** to prevent the wheat and rice infestation in agriculture-based communities. It is widely used in several developing countries like Pakistan, India, Iran, Morocco, Nepal, and many other parts of Asia, especially South Asia.

The lethal dose of wheat pills poisoning is 1-1.5 g. Deaths are reported even with a dose of 150-500 mg.

WHAT IS A WHEAT PILL?

- Commonly available pesticides which are composed of Aluminum Phosphide or Zinc Phosphide.
- The pill is composed of about 44% inert ingredients to prevent decomposition of the tablet, while Aluminium Phosphide is about 56% of the pill. It is also available in the form of pellets, sachets and powder.
- The common trade names include Celphos, Alphos, Quickphos, Phostek, Delicia and Chemfume.

CLINICAL FEATURES

- GI:** Garlic-like odor on breath, nausea, vomiting, thirst, epigastric burning, abdominal cramps or pain, hepatic tenderness, diarrhea, dysphagia, hematemesis (bloody vomiting) and acute pancreatitis.
- CVS:** Hypotension, bradycardia, tachycardia, arrhythmias (abnormal heart rhythms), shock,
- Pulmonary system:** Dyspnea, chest tightness, cough, tachypnea, pulmonary edema, acute respiratory distress syndrome (ARDS) and pleural effusion.
- Renal system:** Oliguria, proteinuria, hematuria, acute renal failure
- CNS:** Anxiety, restlessness, confusion, seizure, coma
- Metabolic:** Hypoglycemia or hyperglycemia, hypomagnesemia, hypokalemia, hyperkalemia, metabolic acidosis.

DIAGNOSTIC WORKUP

- Complete blood count (CBC):** Leukocytosis, Thrombocytopenia, Anemia
- Coagulation profile:** maybe prolonged PT, aPTT & INR in severe toxicity cases, reflecting impaired coagulation.
- Liver function tests (LFTs):** deranged liver enzyme (AST, ALT) – indicative liver toxicity
- Marker of hemolysis:** Elevated level of bilirubin, reticulocytes, LDH and decreased level of haptoglobin.
- Renal function tests (RFTs):** May be elevated BUN and Creatinine – indicative renal dysfunction.
- Basic metabolic panel (BMP):** hypomagnesemia, hypokalemia or hyperkalemia, hypernatremia or hyponatremia, and hypocalcemia.
- Blood glucose levels:** may be decreased (hypoglycemia) or increased (hyperglycemia).
- Serum lactate:** Increased serum lactate levels may be indicative of tissue hypoperfusion and anaerobic metabolism, contributing to metabolic acidosis.
- Arterial blood gas (ABG) analysis:** may reveal metabolic acidosis characterized by a low pH, low bicarbonate (HCO_3^-) levels, and compensatory respiratory alkalosis.
- Cardiac enzymes:** creatine kinase (CK), creatine kinase-MB (CK-MB), and troponin may be elevated in patients with myocardial injury or cardiogenic shock.
- Elevated Serum Amylase and Lipase:** Raised level may suggest pancreatic involvement and pancreatitis.
- Chest x-rays:** may be performed to assess for pulmonary edema, pneumonitis, or other respiratory complications associated with severe poisoning.
- Electrocardiography (ECG):** important to monitor for cardiac abnormalities, such as arrhythmias (e.g., QT prolongation, ventricular tachycardia) and myocardial injury (e.g., ST-segment changes, T-wave abnormalities)
- Silver nitrate test:** for confirm the diagnosis, Silver Nitrate impregnated paper is exposed to the patient's breath or gastric contents, which turns black after exposure to Silver Phosphide, which is formed from the reaction between phosphides and Silver Nitrate. This test strip can be used to check the breath (50% sensitive) and 18 gastric contents (100% sensitive).
- Serial blood levels of Phosphine (PH_3):** Monitored during acute intoxication.



TREATMENT OF WHEAT PILL POISONING (RICE PILL POISONING)

- ☛ Stabilize patients using ABCD&E approach.
- ☛ Make patient Nil per oral (NPO).
- ☛ Consider early HDU/ICU Admission
- ☛ Pass nasogastric (NG) tube and foley's catheter with attach urine bag to record input/output.
- ☛ NO SPECIFIC ANTIDOTE, THE TREATMENT IS MAINLY SUPPORTIVE. EARLY REFERAL TO TERTIARY CARE.
- ☛ **Gastric lavage with potassium permanganate (1:10000) & mineral oil or coconut oil &/or sodium-bicarbonate.**
 - » Gastric lavage was initiated with aliquots of 50 ml of coconut oil and 50 ml of sodium bicarbonate solution and continued for the next half an hour, with simultaneous aspiration being done after every 2–3 minutes through Ryle's tube. Coconut oil was just heated to lukewarm temperature so as to make a miscible solution with sodium bicarbonate. The procedure of gastric lavage was usually done 12–15 times in the first hour.
 - » The initial 30 ml lavage was sent to forensic laboratory for toxicological analysis.
 - » The gastroscope can be used to remove the undissolved pellet.
 - » Water should not be used as a lavage agent. Instead, saline preferred regimen.
- ☛ Establish large-bore intravenous (IV) access.
- ☛ Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂ (Check SpO₂? & Give high flow O₂ as appropriate)
- ☛ Start IV fluids therapy: 0.9% normal saline (NS) & Ringer lactate (RL) or D5%W x IV x BD/TDS
- ☛ Obtained labs: CBC, RFTs, BMP, LFTs, RBS, coagulation profile, ABGs, silver nitrate test & phosphine (PH₃)
- ☛ Enhanced elimination: Enhance the excretion of toxins via urine.
 - » Forced diuresis with diuretics + IV fluid 5–6L.
 - ☛ Inj. Furosemide 40mg/2ml (Lasix) 20mg x IV x TDS. If systolic B.P > 90 mmHg.
 - ☛ Inj. Mannitol 250ml x IV (If the patient is still oligouric).
 - » Urinary alkalinization with intravenous sodium bicarbonate
 - » Hemodialysis: in cases of severe poisoning or renal failure.
- ☛ Gastroprotective: Inj. Omeprazole 40mg (Risek, Ruling) x IV x OD.
- ☛ Antibiotics therapy: Inj. Ceftriaxone 2g (Oxidil, Rocephin) x IV x OD
- ☛ IV corticosteroids: Inj. Hydrocortisone 250mg (Solucortif) at dose 200–400mg x IV, every 4–6 hours, helps to reduce the dose of dopamine & prevents capillary leakage in the lungs to prevent ARDS.
- ☛ For severe metabolic acidosis: IV Sodium Bicarbonate in a dose of 1–1.5 mEq/kg body weight and further adjusted for correction of metabolic acidosis as per ABG reports but empirically to all patients.
- ☛ For hypomagnesemia: IV magnesium sulfate (MgSO₄)
- ☛ For hypotensive shock: plenty of IV fluids and is mostly refractory. IV fluid therapy should be guided by CVP & PCWP. The CVP should be aimed at between 12–14 cm of water. The systolic B.P should be kept > 90mmHg by low renal dose dopamine (at dose 4–6 µg/kg/min) in case of hypotension resistance to fluids.
- ☛ For cardiac arrhythmias (ventricular arrhythmias): Inj. Amiodarone, the dose starts with a loading dose of 150 mg to 300 mg administered intravenously over 10 to 15 minutes, followed by a maintenance infusion of 1 mg to 1.5 mg per minute for 6 hours, and then a maintenance dose of 0.5 mg per minute for 18 hours.
- ☛ For acute liver toxicity: IV N-acetylcysteine (NAC) according to standard protocols
- ☛ With vomiting – consider ONE of the following anti-emetics: Inj. Metoclopramide 10mg/2ml (Metacloclon) x IV x TDS. OR Inj. Ondansetron 8mg/4ml (Onset, Onseron) x diluted in 50 to 100 ml of 0.9% NS OR D5%W, IV over 15 minutes.
- ☛ Identify and treat underlying causes: E.g., Electrolytes imbalance, hypoglycemia, hyperglycemia, ARDS, seizures.
- ☛ Prognosis: Poor prognosis with mortality very high, ranging from 37% to 100%. Most common cause of mortality within 12–24 hours of presentation is usually of a cardiovascular cause such as hypotensive shock and/or arrhythmias. After 24 hours, liver failure is the usual cause of death.
- ☛ Counselling: Explain to caregivers that there's no antidote for wheat pill poisoning, the nature of wheat pills is such that even a seemingly stable patient can deteriorate rapidly and collapse at any moment. Urgent medical attention is essential if there's any change in the patient's condition.
- ☛ Provide psychological support to the patient & their family members, as poisoning incidents can be distressing.

HUMAN BITES

Human bite bacteriologically dirtiest bite
Human bites (which usually occur during fights) lead to infections which, if neglected, almost invariably produce a highly destructive, necrotizing lesion contaminated by a mixture of aerobic and anaerobic organisms.
A deliberately inflicted bite on the hand or elsewhere should be considered as contaminated.

DISCHARGE MEDICATION:

1. Tab. Co-Amoxiclav 1g (Augmentin) x BD
OR Cap. Cefixime 400mg (Cefspan) x OD
2. Tab. Seropeptidase (Danzen DS, Danzen forte) x TDS
3. Tab. Paracetamol 500mg (Panadol, Calpol) 500mg – 1000mg (1-2 tablets) x TDS

Rx

- ☞ **Immediate Firstaid:** The wound should be thoroughly washed and flushed with soap and water (or water alone) for 15 minutes, and disinfected immediately with detergent, iodine, or ethanol.
- ☞ **Vitals monitoring:** Check BP, PR, RR, Temperature, and SpO₂
- ☞ **Tetnus prophylaxis:** Inj. Imatet 0.5ml x IM (Patients who have not received a tetanus vaccine within the past five years)
- ☞ **Give Inj. Hydrocortisone** (Hyzone, Solu-cortif) at dose 100-250mg PLUS Inj. Pheniramine maleate 50mg/2ml (Avil) x IV x STAT
- ☞ **Prophylactic Antibiotics:** Inj Co-Amoxiclav 1.2g (Augmentin) OR Inj Ceftriaxone 1-2g (Oxidil, Rocephin) x IV x STAT
- ☞ **With pain/analgesia**
 - ☞ Inj. Paracetamol 1g/100ml (Provas, Paracet) x IV x TDS/SOS
 - ☞ OR Inj. Ketorolac 30mg/ml (Toradol) in 4ml 0.9% N/S x IV
 - ☞ OR Inj. Tramadol 100mg/2ml (Tramol) + Inj. Dimenhydrinate 50mg/ml (Gravinate) dilute in 100ml 0.9% NS.
- ☞ **Monitoring for Infection:** Patients should be monitored closely for signs of infection, such as redness, swelling, warmth, or drainage from the wound. If signs of infection develop, further evaluation and possibly additional antibiotic therapy may be necessary.
- ☞ Counsel the patient and discharge supportive medication

INSECT BITES / STING BITES

Some people don't notice the insect and may not be aware of a bite or sting until one or more of the following symptoms emerge:

- ☞ Swelling.
- ☞ Redness or rash.
- ☞ Pain in the affected area or in the muscles.
- ☞ Itching.
- ☞ Heat on and around the site of the bite or sting.
- ☞ Numbness or tingling in the affected area.

DISCHARGE MEDICATION

1. Tab. Co-Amoxiclav 1g (Augmentin) x BD
OR Cap. Cefixime 400mg (Cefspan) x OD
2. Tab. Seropeptidase (Danzen DS, Danzen forte) x TDS
3. Tab. Paracetamol 500mg (Panadol, Calpol) 500mg – 1000mg (1-2 tablets) x TDS

Rx

- ☞ **Immediate Firstaid:** Local wound care, cleaning and immobilization of extremity. Place a cold compress or ice pack on the area for about 10 minutes at a time to help reduce pain and swelling. Wrap any ice or ice packs in a clean cloth to protect their skin.
- ☞ **Vitals monitoring:** Check BP, PR, RR, Temperature and SpO₂
- ☞ **IV fluid:** RL OR 0.9% NS x 1L x IV x STAT (If hypotensive patient)
- ☞ **Tetnus prophylaxis:** Inj. Imatet 0.5ml x IM (Patients who have not received a tetanus vaccine within the past five years).
- ☞ **For patient with anaphylaxis:** Give Inj. Hydrocortisone (Hyzone, Solu-cortif) at dose 100-250mg PLUS, Inj. Pheniramine maleate 50mg/2ml (Avil) x IV x STAT
DOC if not respond Inj Adrenaline 0.5ml (1:1000) x IM x SOS
- ☞ **Prophylactic Antibiotics:** Inj Co-Amoxiclav 1.2g (Augmentin) OR Inj Ceftriaxone 1 – 2g (Oxidil, Titan, Rocephin) x IV x OD
- ☞ **With pain/analgesia**
 - ☞ Inj. Paracetamol 1g/100ml (Provas, Paracet) x IV x TDS/SOS
 - ☞ OR Inj. Ketorolac 30mg/ml (Toradol) in 4ml 0.9% N/S x IV
 - ☞ OR Inj. Tramadol 100mg/2ml (Tramol) + Inj. Dimenhydrinate 50mg/ml (Gravinate) dilute in 100ml 0.9% NS.
- ☞ Counsel the patient and discharge supportive medication

DOG BITES (RABIES VIRUS)

THREE CATEGORIES OF DOG BITES EXPOSURE BY WHO

- **Category-I:** Touching/Feeding of animals, Licks on intact skin (No risk of infection if the history is reliable).
- **Category-II:** Nibbling of uncovered skin or minor scratches or abrasions without bleeding (Low risk of infection).
- **Category-III:** Single or multiple transdermal bites or scratches, licks on broken skin, contamination of mucous membrane with saliva from licks, or exposure to bat bites or scratches (High risk of infection).

POST-EXPOSURE PROPHYLAXIS (PEP) – GUIDELINES

- **Category II and III exposures require post-exposure prophylaxis (PEP)**
- **Wound care:** immediately extensive washing of the wound with water and soap for at least 15 minutes and local treatment of the wound as soon as possible after a suspected exposure.
- **The WHO recommends either an intradermal/ID (3-dose) or intramuscular/IM (4-dose or 2-1-1 dose) regimen.**
 - » **The intradermal (ID) regimen is preferred, as this reduces the amount of necessary vaccine and therefore the cost by 60–80% without compromising any safety or efficacy and time-sparing regimen.**
- **The Advisory Committee on Immunization Practices (ACIP):** The Rabies vaccine (1 dose) is given on days 0, 3, 7, and 14 (an additional dose at 28 days is recommended if the patient is immunocompromised) x intramuscular (IM)
- PEP does not have any contraindications, if purified rabies immunoglobulin & rabies vaccine are used. It is recommended in children and pregnant women. If repeat exposure occurs within 3 months of PEP, further PEP is not required.
- **Asymptomatic patient with recent vector exposure (Symptomatic rabies is rare, and almost always fatal).**
 - » **Unimmunized: non-bite exposure with no infection risk** → Reassurance, no risk of infection, treatment not required
 - » **Unimmunized: non-bite exposure with low infection risk** → wound treatment, rabies vaccine and immunoglobulin.
 - » **Unimmunized: bite exposure, licks on broken skin or mucous membrane, or exposure to bat bites or scratches** → wound treatment, rabies vaccine and rabies immunoglobulin.
 - » **Immunized: any exposure with infection risk** → even patients who have been vaccinated against rabies should be treated after exposure! No immunoglobulin. Check antibody titers on day 14.



TREATMENT OF DOG BITES

- **Wound management:** The wound should be thoroughly washed and flushed with soap and water (or water alone) for 15 minutes, and disinfected immediately with detergent, iodine (tincture), or ethanol (700ml/l).
- **POST-EXPOSURE PROPHYLAXIS (PEP)**
 1. **Multiple-dose rabies vaccine (immunization) protocol**
 - » **Un-immunized patient:** Rabies vaccine (Inj. Verorab 0.5ml, Inj. Indirab 0.5ml, Inj. Rabipur 1.0ml)
Dosage: One I/M dose = 0.5ml or 1ml, One I/D dose = 0.1ml, depending on the vaccine manufacturer
 - ↳ **WHO protocols:** Intradermal (3-dose) or intramuscular (4-dose) or (4-dose or 2-1-1 dose) regimen
 - Rabies vaccine at dose 0.1mL (divided between 2 sites) on days 0, 3, and 7 x intradermally (I/D)
 - OR Rabies vaccine 1 dose (at 1-site) on days 0, 3, 7, and between days 14–28 x intramuscular (I/M)
 - OR 2 doses intramuscularly (2-sites) on day 0, followed by an additional dose (1-site) on days 7 and 21
 - ↳ **ACIP protocol:** Rabies vaccine (Inj. Verorab 0.5ml, Inj. Indirab 0.5ml) on days 0, 3, 7, and 14 (and 28 in immunocompromised patients) x intramuscular (IM)
 - » **Immunized patient:**
 - ↳ **WHO protocols:** Rabies vaccine 0.1 mL, 1 dose on days 0 and 3 x ID/IM
 - ↳ **ACIP protocol:** Rabies vaccine 0.5 mL or 1 mL on days 0 and 3 x intramuscularly (IM)
 2. **Rabies immunoglobulin: HRIG 300 I.U./2ml (HyperRAB, Imogam rabies-HT, Berirab-P) OR ERIG 1000 I.U./5ml (Equirab)** is given into the site of the wound by intramuscular (IM) injection
 - ↳ **Human rabies immunoglobulin (HRIG)** at dose 20 IU/kg (0.133 ml/kg)

➤ Patient weight 50 kg x 20 I.U. = 1000 I.U.	➤ 1000 ÷ 150 I.U./ml = 6.7ml
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 - ↳ **Equine rabies immunoglobulin (ERIG):** at dose 40 IU/kg (0.200 ml/kg)

➤ Patient weight 50 kg x 40 I.U. = 2000 I.U.	➤ 2000 ÷ 200 I.U./ml = 10ml
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- **Tetnus prophylaxis:** Inj. Imatet 0.5ml x IM x STAT
- **Analgesia/pain control:** Inj. Diclofenac 75mg x IM OR Inj. Ketorolac 30mg X IV/IM.
- **Counsel the patient and discharge on analgesia ± antibiotics if indicated**
 1. Tab. Co-Amoxiclav 1g (Augmentin, Amclav) x BD OR Cap. Cephalexin 500mg (Ceporex, Keflex) x twice daily (BD)
 2. Tab. Paracetamol 500mg (Panadol, Calpol) x TDS

SNAKE BITES

Most venomous snake bites occur in developing countries.

Not necessarily result in envenomation- even if snake is venomous (up to 30% of bitten patients are not envenomated)

Venomous snake bites are indicated by one or two fang marks on the skin, whereas multiple teeth mark suggests that the snake is not venomous.

Severe local pain, swelling, discoloration developing within 30 mins of bite

Effects of venom

- » Bleeding due to coagulopathy
- » Increase in capillary permeability, which leads to: Local edema & Accumulation of interstitial fluid in the lungs
- » Neuromuscular blockade
- » Cardiac failure can result from hypotension and acidosis.

Conventional dosage schedule of polyvalent anti-snake venom:

- A. Only local swelling, no systemic symptoms: 2-5 units.
- B. Systemic symptoms/ haemorrhagic abnormalities: 5-9 units.
- C. Severe systemic manifestations /shock: 10-15 units.

Discharge medications of Snake

Bites patient

1. Tab. Co-Amoxiclav 1g (Augmentin) x BD
Or Tab. Moxifloxacin 400mg (Avelox, Moxiget) x OD
Or Cap Cefixime 400mg (Cefspan, Cefiget) x OD
 2. Tab. Paracetamol 500mg (Panadol, Calpol) x TDS
- For Swelling/Inflammation
3. Tab. Seropeptidase (Danzen DS, Danzen forte) x TDS
Or Tab. Chymotrypsin (Chymoral Fort) x TDS
 4. Multivitamins (Surbex-z, Vitrum, Revital multi) x OD

Rx

- » Stabilize patient using ABCD&E approach.
- » Establish large-bore intravenous (IV) access.
- » Avoid IM injection – Risk of hematoma formation.
- » Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂ (Check SpO₂ & Give high flow O₂ as appropriate)
- » Obtained labs: CBC, urea, creatinine and electrolytes, LFTs, PT, APTT & INR, Markers of hemolysis (Severe intravascular haemolysis)
- » Consider 'O' Negative blood (universal donor) in emergency.
- » Cross matching with arrange 2 units/Pint of PCVs
- » FFPs if PT/INR is increased OR active bleeding.
- » IV fluid therapy: Ringer Lactate OR 0.9% N/S x 1L x IV x STAT
- » Give Inj. Hydrocortisone (Hyzonate, Solu-cortif) at dose 100-250mg PLUS Inj. Pheniramine maleate 50mg/2ml (Avil) x IV x STAT
- » Inj Imitate 0.5ml x IM, repeat after 4 weeks.
- » Inj Adrenaline 0.5ml (1:1000) x SC, before injection of antivenom to prevent severe acute reactions.
- » Analgesia: Paracetamol 1g/100ml x IV
- » Inj polyvalent anti-snake venom (ASV) 5 vial in 500ml 0.9% N/S x IV x TDS (each vial containing 1 unit of antivenin are made into 10 ml solution).
- » IV Antibiotics: Inj. Co-Amoxiclav 1.2g (Augmentin, Calamox) x IV x BD
OR Inj. Ceftriaxone 1g (Titan, Rocephin) x IV x BD or for Deeper or more serious wound infections Inj. piperacillin-tazobactam 4.5g/vial (Tanzo) x IV x BD/TDS
- » Gastroprotective: Inj. Omeprazole 40mg/vial (Risek, Ruling) x IV x OD
- » For muscle spasms: Inj. Diazepam 10mg (Valium) x IV x SOS
- » Acute renal failure: Try to correct the electrolyte imbalance and give sufficient fluid parenterally. Inj. mannitol (20%) 300 ml is infused over 3 hours or large dose of frusemide (100-200 mg) IV is given. If not corrected by above measures, the patient may require peritoneal or haemodialysis.
- » In Elapidae (cobra) group snake bite: Inj. Neostigmine 0.5mg (1 ml) x IV is given, every half an hour for 4-6 injections until the ptosis or neuro deficit is corrected (The toxin blocks neuromuscular junction). Then IV Inj. neostigmine is given every one hourly & ultimately to be given at 2-3 hours interval till all signs of paralysis have disappeared. Every IV Inj. neostigmine should be preceded by 0.6 mg (1 ampule) of Inj. Atropine given by IV route.
- » Respiratory failure: In respiratory muscle paralysis (by Elapidae group), ventilation by a respirator & proper control of blood gases should be employed.
- » General treatment
 - » Try to identify the snake and refer the victim to nearby hospital.
 - » Only valid first aid- splint extremity; do not cruciate cuts, suck out venom, wrap with ice, or apply band/tourniquet.
 - » Local wound care, cleaning and immobilization of extremity.
 - » Elevating the affected limb to prevent pooling of the venom.
 - » Lately surgical debridement, fasciotomy or skin grafting may be needed.
 - » Obtained ECG for cardiac arrhythmia e.g., Atrial Fibrillation.
 - » As the outcome of snake bite is unpredictable in the initial stage, all cases should be carefully monitored for at least first 12 hours.
 - » Dose of antivenin serum (AVS) in children is either equal or a bit more than the adult dose. Antibiotics covering gram-negative organisms and anaerobes are advocated in local infection.
 - » Re-assure the patient.

CAT BITES

CLINICAL ASSESSMENT

Obtain a Detailed History:

- » Circumstances of the bite (provoked or unprovoked).
- » Time of the bite.
- » Vaccination status of the cat (especially rabies).
- » Any previous medical conditions or medications of the patient.

Examine the Bite Wound:

- » Inspect for depth, location, number of puncture wounds
- » Inspect signs of infection (redness, swelling, warmth, pus).
- » Assess for damage to underlying structures (e.g., tendons, nerves, blood vessels).



- » **Immediate Firstaid:** The wound should be thoroughly washed and flushed with soap and water (or water alone) for 15 minutes, and disinfected immediately with detergent, iodine, or ethanol.

- » **Debridement:** Remove any foreign material and necrotic tissue.
- » **Wound Closure:** Primary closure is generally avoided unless the wound is on the face or if it is a deep puncture wound with a high risk of infection. Leave most bite wounds open to drain.

- » **Tetnus prophylaxis:** Inj. Imatet 0.5ml x IM (Patients who have not received a tetanus vaccine within 5 years)

» Rabies Prophylaxis: see rabies/dog bites

» Assess Rabies Risk:

- » Determine if the biting animal is available for quarantine and observation.
- » If the cat is unavailable or rabies status is uncertain, initiate rabies post-exposure prophylaxis (PEP) as per local health department guidelines.

» Rabies post-exposure prophylaxis (PEP):

- » Administer Rabies immunoglobulin (RIG) infiltrated around the wound and the remainder IM at a site distant from the vaccine.
- » Administer the Rabies vaccine x 4 doses on days 0, 3, 7, and 14.

» Antibiotic Prophylaxis:

- » Tab. Amoxicillin-clavulanate 1g (Augmentin) x orally twice daily (BD)

» OR Alternatives for Penicillin-Allergic Patients:

- Cap. Doxycycline 100 mg (Doxyn) x orally twice daily (BD)
PLUS, Tab. Metronidazole 500 mg (Flagyl) x orally three times daily (TDS).
- Cap. Clindamycin 300 mg (Dalacin-C) orally four times daily (QID)
PLUS, Tab. Ciprofloxacin 500 mg (Novidate) x orally twice daily (BD).

» Indications for Antibiotics:

1. Deep puncture wounds.
2. Bites on the hands, face, or genitals.
3. Bites in immunocompromised patients (e.g., diabetes, HIV/AIDS, chemotherapy).
4. Presence of signs of infection at the time of presentation.

- » **Monitoring for Infection:** Patients should be monitored closely for signs of infection, such as redness, swelling, warmth, or drainage from the wound. If signs of infection develop, further evaluation and possibly additional antibiotic therapy may be necessary.

- » Counsel the patient and discharge supportive medication

HYPOKALEMIA

- Definition:** Hypokalemia = Serum K⁺ level < 3.5 mEq/L. **Severe hypokalemia** = Serum K⁺ level < 2.5 mEq/L
- Clinical features:** Patients may be asymptomatic, particularly if the deficiency is mild. Symptoms usually occur if serum K⁺ levels are < 3.0 mEq/L and/or decrease rapidly.
- Cardiovascular features:** Symptoms of arrhythmias (Palpitation, Irregular pulse, Syncope) and Hypotension
 - ECG findings:** Flattened T waves, ST depression, Presence of U waves
 - Neuromuscular manifestations:** Muscle cramps and spasms, Muscle weakness, paralysis, Respiratory failure secondary to paralysis of respiratory muscles, Rhabdomyolysis, Decreased deep tendon reflexes
 - GIT manifestations:** Fatigue, Nausea, vomiting, constipation or ileus
 - Other manifestations:** Polyuria, Hyperglycemia
 - Symptoms of underlying causes:**
 - Dehydration in gastroenteritis
 - Tachycardia and tremors in alcohol withdrawal
 - Symptoms of thyrotoxicosis
 - Symptoms of digoxin toxicity in patients treated with digoxin



TREATMENT OF HYPOKALEMIA

- Stabilize patients using ABCD&E approach.
- Establish large-bore intravenous (IV) access.
- Vitals monitoring: monitor BP, PR, RR, Temperature, check SpO₂ & Give high flow O₂ as appropriate.
- Obtain labs: CBC, Urea, Creatinine, Electrolytes, LFTs, Calcium, Magnesium, Phosphate and ABGs.
- IV fluid to correct electrolyte abnormalities.
- IV Potassium replacement → Inj. Potassium chloride (KCL)
 - Available strength: 10meq, 20meq, 30meq, 40meq
 - Compatible solution: 0.9% NS, D5%W
 - Dilution:

KCL INFUSION TABLE (PERIPHERAL LINE)

10meq KCL in 500ml solution Final concentration: 1meq/50ml		20meq KCL in 500ml solution Final concentration: 1meq/25ml	
Dose in meq/hr	ml/hr	Dose in meq/hr	ml/hr
2	50	2	100
4	100	4	200
6	150	6	300
8	200	8	400

- Deficit formula: $0.4 \times \text{weight} \times (\text{Desired value} - \text{patients value})$
- Diuretic-induced hypokalemia:** Discontinue diuretic drugs.
- Continuous cardiac monitoring and ECG for Cardiac arrhythmia
- Mild Case:** Consider Syp. Potassium chloride (K-Lyte) x PO x 2-TSP x BD/TDS in half cup water, Or/& Tab Potassium chloride 500mg (New-K) x 2-6 tablets x BD/TDS.
- Consider measuring urinary potassium.
- Identify and treat underlying etiology. E.g. Consider IV magnesium for patients with hypomagnesemia.
- Oral potassium supplementation:** Consider increasing dietary potassium intake → e.g., bananas, yogurt etc.

REPLETION REGIMENS FOR HYPOKALEMIA

Serum Potassium level	Recommended regimen
< 2.5 mEq/L and/or symptomatic	- IV KCL via central line - Maximum rate of 40 mEq/hour recommended for central line
2.5 mEq/L–2.9 mEq/L and/or unable to tolerate per orally	- IV KCL via peripheral line - Maximum rate of 10 mEq/hour recommended for peripheral IV
3.0–3.4 mEq/L	Oral potassium chloride, Consider oral potassium bicarbonate, if hypokalemia is due to metabolic acidosis.
≥ 3.5 mEq/L	Repletion generally not necessary. Consider oral potassium chloride for patients with DKA, CHF, and/or undergoing active diuresis

HYPERKALEMIA

- ☞ Normal potassium (K^+) level: = 3.5-5.0 mmol/L (3.5-5.0 mEq/L)
- ☞ Hyperkalemia: = K^+ level >5.0 mmol/L (5.0 mEq/L)
 - » Mild: 5.5-5.9
 - » Moderate: 6.0-6.4
 - » Severe: >6.5
- ☞ Clinical presentation:
 - » Muscle weakness: Paralysis, Paresthesia
 - » decrease deep tendon reflexes
 - » Nausea, vomiting
 - » Diarrhea
 - » Tachycardia, palpitations
 - » Cardiac arrhythmias in very severe cases: Atrioventricular (AV) block, ventricular fibrillation



TREATMENT OF HYPERKALEMIA

- ☞ Stabilize patients using ABCD&E approach.
- ☞ Establish large-bore intravenous (IV) access.
- ☞ Vitals monitoring: Check BP, PR, RR, Temperature, SpO₂
- ☞ IV Fluid: 0.9% Normal saline, dextrose 5% x IV STAT
- ☞ Initial Assessment:
 - » Confirm Diagnosis: Measure serum potassium levels.
 - » Assess Severity: Check ECG for changes (e.g., peaked T waves, widened QRS).
- ☞ Stabilize cardiac membrane: If there is evidence of ECG changes in hyperkalemia, calcium salts reduce cardiac irritability.
 - » Inj. Calcium Gluconate 10%/10ml: 1 g IV over 2-5 minutes (repeat every 10-20 minutes if needed).
 - » Inj. Calcium Chloride: 500 mg to 1 g IV over 5-10 minutes (alternative to gluconate; use with caution due to irritant properties).
- ☞ Shift Potassium Intracellularly:
 - » Short acting regular Insulin + Glucose: Regular Insulin (Humulin-R, Insuget) at dose 10 I.U in combination with Dextrose 25%/25ml x 4 ampule in 100ml IV chamber administer over 30 minutes
 - ❖ OR Consider HyperK-Cocktail infusion local protocol: (off label)
Short acting Regular insulin 10 I.U + Inj Calcium gluconate 10%/10ml + Dextrose 25%/25ml x 4 ampule, all mention drugs should be put in 100ml IV chamber (100ml burette infusion set) x IV STAT over 30 min
 - » Inhaled SABA (Beta-2-adrenergic agonists): Nebulize Salbutamol 5mg/ml (Ventolin solution) at dose 10-20mg once, consider as adjunctive to insulin.
 - » IV Sodium Bicarbonate 7.5%/50ml: 50-100 mEq IV bolus, (if metabolic acidosis is present)
- ☞ Remove Potassium from the Body:
 - » Diuretics: Inj. Furosemide 20mg/2ml (Lasix) at dose 20-80 mg IV bolus.
 - » Dialysis: Consider if severe or persistent hyperkalemia.
- ☞ Sodium Polystyrene Sulfonates (Kayexalate):
 - » Oral Administration: Dose: 15 g in 60 mL of plain water once daily or every 6-12 hours.
 - » Rectal Enema:
 - ↳ Dose: 30-50 g in 80 mL every 6 hours.
 - ↳ Retention Time: Keep the suspension in the colon for at least 30-60 minutes, or longer if possible.
- ☞ Correct underlying causes: Address potential causes such as medication effects, renal injury, or adrenal issues.
- ☞ Monitor and Reassess:
 - » Repeat Labs: Regularly check serum potassium levels and ECG.
 - » Continuous Monitoring: Track vital signs and ECG changes.
- ☞ Follow-Up Care: Chronic Management: Implement dietary changes and adjust medications as needed for long-term potassium control.

HYPOGLYCEMIA

CLINICAL FEATURES

Hypoglycemia: Blood sugar level <70 mg/dL (3.9 mmol/L).

Threshold for symptoms

- Varies greatly, but symptoms have usually occurred when serum glucose level is <50 mg/dL (2.8 mmol/L)
- The threshold at which symptoms may appear in patients with chronic diabetes is especially variable due to hypoglycemia-associated autonomic failure (HAAF).
 - Recurrent hypoglycemia $\rightarrow$ changes in the counter regulatory response (e.g., decreased epinephrine release) $\rightarrow$ lower glucose threshold needed to trigger symptoms $\rightarrow$ asymptomatic hypoglycemia
 - For this reason, the initial symptoms of hypoglycemia in patients with HAAF is often confusion.
- The threshold can also vary due to medication: Beta blockers can mask signs of hypoglycemia.

Signs and symptoms

- Neurogenic/autonomic**
 - Increased sympathetic activity: tremor, pallor, anxiety, tachycardia, sweating, and palpitations
 - Increased parasympathetic activity: hunger, paresthesias, nausea, and vomiting
- Neuroglycopenic:** Agitation, confusion, behavioral changes, Fatigue, Seizure, focal neurological signs (Somnolence $\rightarrow$ obtundation $\rightarrow$ stupor $\rightarrow$ coma)

DIAGNOSTIC APPROACH

1. Confirm low blood glucose (via fingerstick,) and check for Whipple triad.
 2. Rule out acute illness as a cause (e.g., infection, sepsis, burns).
 3. Review the patient's medications to rule out medication as a cause (see drugs that cause hypoglycemia).
 4. Perform diagnostic workup based on the leading differential diagnosis & whether the patient has DM or not
- ❖ If the Whipple triad is not confirmed, no further workup is indicated.
- **Diabetic patients:** Hypoglycemia in diabetic patients is almost always due to acute illness and/or medications (e.g., insulin) and further workup is generally not indicated.
- Initial workup if no obvious trigger identified:**
- » **Laboratory tests:** CBC, Urea, creatinine, electrolytes, RBS/FBS, LFTs, ABGs and urinalysis
 - » **Radiology:** X-ray chest, CT & MRI Brain (combined ix is required to confirm the diagnosis of insulinoma)
 - » **Infectious workup:** Blood C&S, Urine C&S
 - » Consider sulfonyleurea and exogenous insulin levels.
- **Nondiabetic patients:** Rule out acute illness and medication as a cause. Further diagnostic testing should only be pursued if the cause is not evident based on history and examination (and with the guidance of an endocrinologist). The goal is to determine if the hypoglycemia is due to hyperinsulinemia (e.g., insulinoma).

TREATMENT OF HYPOGLYCEMIA



Suspected severe hypoglycemia should be treated immediately, without waiting for the results of blood glucose testing!

- Stabilize patients using ABCD&E approach.
- Establish large-bore intravenous (IV) access.
- **Vitals monitoring:** Check BP, PR, RR, Temperature, SpO₂ (Check SpO₂ & Give high flow O₂ as appropriate)
- **Obtained labs:** CBC, BUN, creatinine, electrolytes, LFTs, insulin, proinsulin and C-peptide as well as a 72 hour fast (gold standard for diagnosis of insulinoma).
- If RBS ≤ 70 , immediately give Inj. Dextrose 25%/25ml/ampule at 100-150ml (4-6 ampule = 100-150%) x IV x STAT
- If patient is alert, offer an oral or liquid source of glucose (sugary food and drinks): 1/2 glass of fruit juice, teaspoons of sugar or honey, 6 or 7 jellybeans or hard candies, Premeasured glucose tabs or gel (Glucogel)
- Inj. D5%W 1L + IV thiamine (Inj Neurobion 2 ampules) x IV x STAT
- In severe cases consider Inj. glucagon: (Gvoke HypoPen 0.5mg/0.1ml, Gvoke HypoPen 1mg/0.2ml) x subcutaneous (CS) in lower abdomen, outer thigh, or outer upper arm. if neither oral or IV routes of administering glucose are feasible. **Pharmacodynamics:** After administration of 1 mg GVOKE in adult patients with diabetes, the mean maximum glucose increase from baseline was 176 mg/dL.
- **With seizures:** Give Inj. Diazepam 10mg/2ml (Valium) x 10mg diluted in 8ml 0.9% NS OR D5%W x at dose 2mg up to 10mg x IV. For seizures prophylaxis: Inj. Levetiracetam 500mg/5ml (Lerace, Epilapsa) at dose 1-2g in 100ml 0.9% NS x IV over 15-20 minutes.
- Recheck bedside glucose every 30-40 minutes & Titrate dextrose infusion to maintain serum glucose >100 mg/dL.

HEAT STROKE

Clinical Assessment

- » **History:**
 - » Document exposure to high temperatures or strenuous physical activity in a hot environment.
 - » **Symptoms:** Identify classic symptoms such as altered mental status, confusion, seizures, loss of consciousness, or coma.
- » **Physical Examination:**
 - » **Vital Signs:**
 - ↳ Elevated core body temperature, usually above 40°C (104°F).
 - ↳ Tachycardia (rapid heart rate).
 - ↳ Hypotension (low blood pressure).
 - » **CNS Exam:** Altered mental status or disorientation, seizures, focal neurological deficits, loss of consciousness.
 - » **Skin Assessment:**
 - ↳ Hot, dry skin (absence of sweating in classic heat stroke).
 - ↳ Sweating may be present in exertional heat stroke.
- » **Laboratory Tests:**
 1. **Basic Metabolic Panel:**
 - ↳ Electrolyte imbalances (e.g., hyponatremia, hypokalemia).
 - ↳ Elevated blood urea nitrogen (BUN) and creatinine levels (indicating renal dysfunction).
 2. **CBC:** Leukocytosis (elevated WBC count), Low Platelet count if there is DIC
 3. **Liver Function Tests (LFTs):** Elevated transaminases (AST and ALT) indicating hepatic injury.
 4. **Coagulation Profile:** Prolonged prothrombin time (PT) and activated partial thromboplastin time (aPTT).
 5. **Arterial Blood Gases (ABGs):** Metabolic acidosis or respiratory alkalosis.
 6. **Creatine Kinase (CK):** Elevated levels indicating rhabdomyolysis.
 7. **Urinalysis:** Myoglobinuria (presence of myoglobin in urine) indicating muscle breakdown.
 8. **Serum troponin:** Elevated levels indicating potential myocardial injury/cardiomyopathy
- » **Imaging:**
 - » **Chest X-ray:** Assess for pulmonary edema or other complications.
 - » **CT scan head:** Evaluate for cerebral edema or other intracranial pathology if altered mental status persists.
 - » **Electrocardiogram (ECG):** Monitor for cardiac arrhythmias.



MANAGEMENT OF HEAT STROKE

- » Stabilize patients using ABCD&E approach.
- » Establish large-bore intravenous (IV) access.
- » **Vitals monitoring:** Check BP, PR, RR, Temperature, SpO₂ (Check SpO₂ & Give high flow O₂ as appropriate).
- » **Obtained labs:** CBC, Urea, creatinine and electrolytes, LFTs, troponin, coagulation profile and ABGs.
- » **Heat Stroke Management Protocol**
 - 1) **Prehospital Care:**
 - » **Remove from Hot Environment:**
 - ↳ Move the patient to a cooler area immediately.
 - ↳ Perform standard resuscitation measures.
 - » **Initial Assessment:**
 - ↳ Check point-of-care glucose/bed side RBS, if there is altered mental status.
 - ↳ Monitor vital signs and level of consciousness.
 - » **Cooling Measures:**
 - ↳ Remove clothing.
 - ↳ Use one of the following methods:
 - Spray the patient with water and provide airflow.
 - Place wet towels or sheets over the body.
 - Place ice packs on the neck, armpits, and groin.



- » **Fluid Resuscitation:** Administer a bolus of crystalloids (normal saline) – 1-2L, if hypotension is present.
- » **Medical Direction:** Consult online medical direction if transport times are long or if heat stroke cases are rare in the region.
- 2) **Emergency department (ED) Resuscitation:**
 - » **Goals:** 1. Immediate cooling. 2. Aggressive support of organ system function.
 - » **Standard Resuscitation:**
 - ✎ Continue standard resuscitation measures.
 - ✎ Administer IV fluids to ensure adequate urine output.
 - ✎ In elderly patients or those with cardiovascular disease, consider invasive monitoring.
 - » **Monitoring:** Check glucose levels. Monitor core temperature with an electronic rectal thermometer, temperature probe-equipped urinary drainage catheter, or esophageal thermometer.
- 3) **Cooling Techniques:**
 1. **Evaporative Cooling:**
 - » Remove patient clothing.
 - » Spray cool water (~15°C [59°F]) on the patient's body.
 - » Use a fan to facilitate evaporation.
 - » Consider tepid water (40°C [104°F]) to prevent shivering.
 2. **Immersion Cooling:**
 - » Place the undressed patient in a tub of ice water deep enough to cover the trunk and extremities.
 - » Ensure the patient's head remains out of the water.
 - » Be aware of potential issues such as shivering, monitoring lead displacement, and resuscitative procedure limitations.
 3. **Invasive Cooling Measures (if other methods are insufficient):**
 - » Cardiopulmonary bypass (most rapid but limited by availability and logistics).
 - » Cold water gastric lavage.
 - » Cold water urinary bladder lavage.
 - » Cold water rectal lavage.
 - » Cold water peritoneal lavage (effectiveness not validated).
 4. **Other Cooling Measures:**
 - » Cooling blankets (slow, not sole treatment).
 - » IV infusion of cold fluids (not effective alone).
 - » Applying ice packs to the neck, axillae, and groin (not quick enough alone).
 - » Antipyretics are not effective.
 - » Dantrolene is not indicated.
- 4) **Post-Cooling Monitoring and Care:**
 - » **Avoid Hypothermic Overshoot:**
 - ✎ Aim to reduce core temperature to approximately 39°C (102.2°F).
 - ✎ Continuously monitor core temperature to avoid overshoot hypothermia.
 - » **Supportive Care:**
 - ✎ Consider benzodiazepines for shivering and seizures.
 - ✎ Address any complications related to organ dysfunction.
 - ✎ Monitor for and treat delayed complications (e.g., management of rhabdomyolysis).
 - » **Continue cooling until:**
 - Normal body temperature
 - Clinically stable with normal CNS function
 - ✎ Provide ongoing supportive care as needed.
- 5) **Disposition**
 - » All patients require hospital admission.
 - » Most patients require ICU admission to monitor and manage organ failure.
- 6) **Complications:** 1. Multisystem organ failure, 2. Acute respiratory distress syndrome, 3. Rhabdomyolysis and acute kidney injury, 4. Acute hepatic dysfunction, 5. Disseminated intravascular coagulation
- ❖ Antipyretics interrupt the change in the hypothalamic set point caused by pyrogens and are ineffective in heatstroke. They may even be harmful because of the risk of bleeding.

Non-steroidal anti-inflammatory drugs (NSAIDs)/Analgesic/Antipyretics/Opioids analgesics

Generic	Brand name & strength	Dosage
Aspirin	» Tab Disprin 300mg	TDS/ QID
Paracetamol (Acetaminophen)	» Tab Panadol 500mg, Tab Calpol 500mg	
	» Syp Panadol 160mg/5ml, Syp Calpol 120mg/5ml	
	» Syp Panadol Forte 250mg/5ml (see paediatric dosages)	
	» Syp Calpol 6 plus 250mg/5ml	
	» Infant drops: Panadol drop, Tempol plus drop	
	» IV Infusion: Inj. Provas 1g/100ml, Inj. Bofalgan 1g/100ml, Inj. Nubrol-P 1g/100ml	
	» Napa suppository 125mg, 250mg, and 500mg	TDS
Paracetamol + Caffeine	» Tab Panadol Extra, Tab Calpol plus	
Paracetamol + Pseudoephedrine + Chlorpheniramine maleate	» Tab Panadol CF	
	» Tab Reltus CF, Syp Reltus CF	
Paracetamol + Diphenhydramine + Phenylephrine	» Tab Provas EZ	
Paracetamol + Codeine phosphate + Caffeine	» Tab Napadoc	
Paracetamol + Codeine phosphate	» Tab Codogesic	
Paracetamol 200mg + Pholcodine 3.33mg Pseudoephedrine 13.33 mg	» Syp Daycor	BD/TDS
Paracetamol 500mg+ Ibuprofen 200mg	» Tab Provas Duo	
Paracetamol + Orphenadrine citrate	» Tab Nubrol, Tab Nubrol forte	
	» Tab. Sinaxamol, Tab. Sinaxamol forte	
Paracetamol + Thioridazine + caffeine	» Tab Diagesic-P	
Paracetamol 325mg + Tramadol 37.5mg	» Tab Tramol plus, Tab. Tonoflex-P	
Paracetamol 650mg + Tramadol 80mg	» Tab Tramol plus forte, Tab Tonoflex-P forte,	
Ibuprofen	» Brufen topical cream	TDS/QID
	» Tab Brufen 200mg, Tab. Brufen 400mg	
	» Syp Brufen (100mg), Syp Brufen DS (200mg)	
	» IV infusion 400mg/100ml: Inj. Inbufin, Inj. Boschufen	
	» Inj Xaleve 400mg/4ml (dilute in 100ml NS x IV)	
Dexibuprofen	» Tab Tercica 200mg, 300mg, and 400mg	TDS
	» Tab Hifen 300mg, Tab Hifen x 400mg	
	» Syp Tercica 100mg/5ml, Syp Hifen x 100mg/5ml	
	» Tab Brufen Plus, Tab Migofen	
	» Tab Arinac, Tab Rhinoff	
Ibuprofen + codeine phosphate	» Tab Arinac forte, Tab Rhinoff forte	
Ibuprofen 200mg+Pseudoephedrine 30mg	» Syp Arinac, Syp Rhinoff	
Ibuprofen 400mg+Pseudoephedrine 60mg	» Syp Ponstan, Syp Dollor, Syp Gardan	
Ibuprofen 100mg+Pseudoephedrine 15mg	» Tab Ponstan, Tab Dollor, Tab Gardan	
Mefenamic acid 50mg/5ml syrup	» Tab. Ponstan forte, Tab. Dollor DS, Tab Gardan forte	
Mefenamic acid 250mg tablets	» Tab Voltal 25mg, Tab Voren 25mg	TDS
Mefenamic acid 500mg tablets	» Tab Voltal 50mg, Tab Voren 50mg, Tab Dicloran 50mg	
Diclofenac sodium	» Tab Voren 75mg, Tab Dicloran 75mg, Tab. Arnil 75mg	BD/TDS
	» Tab Voltal 100mg, Tab Voren & Dicloran 100mg	BD
	» Inj Voren, Inj Voltal, Inj Artifen, Inj Dyclo	OD/BD
Diclofenac sodium 75mg/3ml injection		BD

Diclofenac diethyl ammonium salt 2gm gel	» Voltral Emulgel, Dicloran gel, Artifen gel	TDS/QID
Diclofenac potassium	» Tab Caflam 50mg, Diclorep 50mg, Tab Maxit 50mg	BD
Indomethacin	» Cap Indobid 25mg	BD/TDS
Naproxen Sodium	» Tab Neoprox 250mg, Tab Flexin 250mg, Proxen 250mg	TDS/QID
	» Tab. Anex 275mg, Tab. Aproxen 275mg	
	» Tab Neoprox 500mg, Tab Flexin 500mg, Proxen 500mg	
	» Tab Synflex 550mg, Tab. Anex 550mg, Aproxen 550mg	BD
	» Tab Acenac 100mg, Tab. Alkeris 100mg	
Acetoclofenac	» Cap Acenac SR 200mg, Tab. Alkeris 200mg	OD
	» Inj Acenac 15mg/vial x IM	BD
	» Acenac topical gel, Alkeris topical gel	TDS/QID
Flurbiprofen	» Tab Froben 50mg	BD/TDS
	» Tab Froben 100mg, Tab Ansaïd & Inflatix 100mg	BD
	» Cap Froben SR (200mg), Cap Inflatix SR 200mg	OD
	» Froben 5% topical gel	TDS/QID
Ketoprofen	» Tab. Profenid EC (100mg), Tab. Proket 100mg	BD
	» Tab. Profenid SR (200mg), Tab. Ketoflex 200mg	OD
	» Dowfen gel, Fastum gel, Ketoflex gel	TDS/QID
	» Profenid 50mg/2ml x IM	BD
	» KefenTech 30mg Patch (Plaster)	TDS
Nimesulide	» Tab Unix 100mg, Tab Nims 100mg	BD
Meloxicam	» Tab Melfix 7.5mg, Tab Mobix 7.5 mg	
	» Tab Melfix 15mg, Tab Mobix 15mg	OD
Piroxicam	» Cap Feldene 20mg, Tab Feldene 20mg	
	» Cap Pcam 20mg, Tab. Pcam 20mg	BD
	» Inj. Pcam 20mg/1ml x IM	
	» Feldene topical gel, Pcam topical gel	TDS/QID
Lornoxicam	» Tab Acabel 4mg, Tab. Loxibar 4mg	BD
	» Tab. Acabel 8mg, Tab Atcam 8mg, Tab. Xikarapid 8mg	
	» Tab. Loxibar 8mg, Tab. Orno 8mg, Tab. Zafon fast 8mg	OD/BD
	» Inj Orno 8mg/vial, Inj. Acabel 8mg/vial x IM/IV	
Piroxicam + Beta Cyclodextrin	» Tab Brexin 20mg, Tab Briax 20mg	BD
Celecoxib	» Cap Celbexx 100mg, Cap Nuzib 100mg & Cap Moveryl	
	» Cap Celbexx 200mg, Cap Nuzib 200mg & Cap Moveryl	OD/BD
Diacerein 50mg	» Cap Diarox 50mg, Cap Diora 50mg	
Etoricoxib	» Tab Flexia 60mg, Tab Etoxib 60mg	OD
	» Tab Starcox 60mg, Starcox 90mg & Starcox 120mg	
Ketorolac 30mg per 1 ml	» Inj. Toradol, Inj. Tekac, Inj. Ketor	TDS/QID
Ketorolac 10mg	» Tab. Toradol 10mg, Tab. Kelac 10mg	TDS/QID
Tramadol	» Cap. Tramol 50mg, Cap. Tonoflex 50mg	TDS/QID
	» Tab Tramol SR 100mg, Tab. Tonoflex SR 100mg	BD/TDS
	» Inj Tramol 100mg/2ml x IV/IM	TDS/QID
	» Inj. Tonoflex 100mg/2ml x IV/IM	
Tapentadol 75mg	» Tab Tapento IR 75mg, Tab Tydel 75mg	BD/TDS
Morphine sulphate	» Cap. Magnus MR 10mg, Cap Magnus MR 30mg	BD/TDS
Buprenorphine 0.3mg = 300mcg per 1 ml	» Inj. Buepron 0.3mg/1ml, Inj Norpin 0.3mg/1ml	TDS/QID
Buprenorphine 0.2mg = 200mcg	» Tab. Bunorfin 0.2mg (200mcg), Tab Zonor	
Pentazocine 30mg/1ml injection	» Inj. Pentazogon 30mg/1ml, Inj Sosegon 30mg/1ml	
Pentazocine 25mg tablets	» Tab. Sosegon 25mg	TDS/QID
Nalbuphine	» Inj. Kinz 10mg/1ml, Inj. Kinz 20mg/1ml	
	» Inj. Nubin 10mg/1ml, Inj. Nubin 20mg/1ml	

ANTIBIOTICS

Generic	Brand name & strength	Dosage
Penicillin-G Benzathine	» Benzibiotic 1.2 million/vial	
Ampicillin	» Cap Penbritin 500mg	
	» IV Injection: Inj. Penbritin 500mg/vial	TDS
Amoxicillin	» Cap Amoxil 500mg, Cap Zeemox 500mg, Cap Wymox 500mg	
	» Tab. Zeemox 1g, Tab. Ospamox 1g	TDS
	» IV Injection 500mg/vial and 1g/vial: Amoxil, Zeemox, zoxicillin	BD
Ampicillin + Cloxacillin	» IV Injection 500mg/vial and 1g/vial: Amoxil, Zeemox, zoxicillin	
Piperacillin + Tazobactam	» Cap. Ampiclox 500mg	
	» Inj. Tazocin EF 4.5g/vial, Inj. Tanzo 4.5g/vial	TDS
Amoxicillin + Sulbactam	» Inj. Talzon 4.5g/vial, Inj. Pencital 4.5g/vial	TDS/QID
Co-Amoxiclave	» Inj. Bactamox 1.5g/vial, 3g/vial	TDS/QID
(Amoxicillin + Clavulanate Potassium)	» Tab. Augmentin 375mg, Tab. Calamox 375mg, Tab. Amclav 375mg	TDS
	» Tab. Augmentin 625mg, Tab. Calamox 625mg, Tab. Amclav 625mg	
	» Tab. Augmentin 1g, Tab. Calamox 1g, Tab. Amclav 1g	
	» Inj. Augmentin 1.2g, Inj. Amclav 1.2g, Inj. Zamoclav 1.2g	BD
Pipemidic acid	» Tab Urixin 400mg	
Nalidixic acid	» Tab Negram 500mg, Tab Nilacid 500mg	TDS/QID
Enoxacin	» Tab Enoxabid 400mg, Cap Enoxazan 400mg	
Ofloxacin	» Tab Tarivid 200mg, Tab Ofiobid 200mg, Tab Oflox 200mg	BD
	» Tab Oflobid 400mg, Tab Oflox 400mg, Tab. Tariflox 400mg	
	» IV infusion 200mg/100ml: Inj. Tarivid, Inj. Oflobid, Inj. Tariflox	
Ciprofloxacin	» Tab Ciproxen 250mg, Tab Novidate 250mg, Tab. Hiflox 250mg	TDS
	» Tab Ciproxen 500mg, Tab Novidate 500mg, Tab. Hiflox 500mg	BD
	» Tab Novidate 750mg, Tab. Hiflox 750mg, Tab Quinoflox 750mg	
	» Tab Novidate XR 500mg, Tab Novidate XR 1000mg	OD
	» IV infusion 200mg/100ml: Inj. Novidate, Inj. Cipesta, Inj. Quinoflox	BD/TDS
	» IV infusion 400mg/100ml: Inj. Novidate DS, Cipesta DS, Quinoflox DS	
Norfloxacin	» Tab Noroxin 400mg, Tab Utinor 400mg, Tab Bectinor 400mg	
Sparfloxacin	» Tab Sparaxin 100mg, Tab Quspar 100mg	BD
Levofloxacin	» Tab Leflox 250mg, Tab Qumic 250mg, Tab. Effiflox 250mg	
	» Tab Leflox 500mg, Tab Qumic 500mg, Tab. Effiflox 500mg	
	» Tab Leflox 750mg, Tab Qumic 750mg	
	» IV infusion 500mg/100ml: Inj. Leflox, Inj. Qumic, Inj. Effiflox	
	» IV infusion 750mg/150ml: Inj. Leflox 750mg/150ml	OD
Gemifloxacin	» Tab Floxigem 320mg, Tab Gemi 320mg, Tab Actigem 320mg	
Moxifloxacin	» Tab Xefecta 400mg, Tab Avelox 400mg, Tab Moxiget 400mg	
	» IV infusion 400mg/250ml: Inj. Avelox, Inj. Moxiget, inj. Avelin	
Cefadroxil	» Cap Duricef 500mg, Cap/Tab Cedrox 250mg mg, Cap Dromax 250mg	TDS
	» Cap Duricef 500mg, Cap/Tab Cedrox BD (500mg), Cap Dromax 500mg	BD
	» Tab Cedrox 1g, Tab. Dromax 1g	OD/BD
Cephalexin	» Cap Ceporex 250mg, Cap Keflex 250mg	TDS/QID
	» Cap Ceporex 500mg, Cap Keflex 500mg	BD
	» Cap Velocef 250mg, Cap Vericef 250mg, Cap Cefresh 250mg	TDS/QID
Cephadrine	» Cap Velocef 500mg, Cap Vericef 500mg, Cap Cefresh 500mg	BD/TDS
	» Inj Velocef 1g/vial, Inj Vericef 1g/vial Inj Cefresh 1g/vial	BD/TDS
	» Inj Kefzol 1g/vial	BD/TDS
Cefazoline	» Cap Ceclor 250mg, Cap Cefalor 250mg, Cap Slate 250mg	TDS



Cefaclor	» Cap Ceflor 500mg, Cap Ceflor 500mg, Cap Slate 500mg	BD
	» Tab. Ceflor MR 375mg, Tab. Ceflor MR 750mg	
Cefuroxime	» Tab Zinacef 250mg (Usual dose: 250 – 500mg PO x twice daily)	BD
	» Inj Zinacef 750mg, Inj Zinacef 1g	
Cefixime	» Cap Cefim 200mg, Cap/Tab Cebosh 200mg, Tab Cefiget 200mg	BD
	» Cap Cefspan 400mg, Cap Cefim 400mg, Cap Cefiget 400mg,	
	» Cap Cebosh 400mg, Tab Cebosh 400mg, Cap Mixel 400mg	
Ceftazidime	» Inj Fortum 1g, Inj Fortazim 1g, Inj Ceftiz 1g	BD/TDS
Cefotaxime	» Inj Claforan 1g/vial, Inj Cefotax 1g/vial, Inj wintax 1g/vial	TDS
Ceftizoxime	» Inj Tezox 1g/vial	BD/TDS
Ceftriaxone	» Inj Oxidil 1g/vial, Inj Titan 1g/vial, Inj Cefxone 1g/vial	BD
	» Inj Rocephin 1g/vial, Inj Cefiro 1g/vial	
	» Inj Oxidil 2g/vial, Inj Titan 2g/vial	
	» Inj Cefxone 2g/vial, Inj Cefiro 2g/vial	
Cefpodoxime	» Tab Abacus 100mg, Tab Abacus 200mg	BD
	» Tab Prelox 100mg, Tab Orelox 100mg	
Cefdinir	» Cap Dinacor 300mg, Cap Neonir 300mg, Cap Efdir 300mg	BD
Cefoperazone	» Inj Cefobid 1g/vial, Inj Cefobid 2g/vial	BD
Cefoperazone + Sulbactam	» Inj 2SUM 1g/vial, Inj Cebac 1g/vial	BD
	» Inj Psulb 1g/vial, Inj Xorbact 1g/vial	
	» Inj 2SUM 2g/vial, Inj Cebac 2g/vial	
	» Inj Psulb 2g/vial, Inj Xorbact 2g/vial	
Cefepime	» Inj Cefstar 1g/vial, Inj Uceph 1g/vial, Inj Maxum 2g/vial	BD/TDS
Cefpirome	» Inj Ivcef 1g/vial (1- 2g x twice daily)	TDS
Erythromycin	» Tab Erythrocin 500	BD
	» Inj Erythrocin 1g	
Azithromycin	» Cap Azomax 250mg, Cap Macrobac 250mg, Tab Azitma 250mg	BD
	» Tab Azomax 500mg, Tab Macrobac 500mg, Tab Azitma 500mg	
	» Inj Azitma 500mg/vial, Inj Zerot 500mg/vial	
Clarithromycin	» Tab Klaricid 250mg, Tab Claritek 250mg, Tab Rithmo 250mg	BD/TDS
	» Tab Klaricid 500mg, Tab Claritek 500mg, Tab Rithmo 500mg	
	» Tab Klaricid XL 500mg, Tab Claritek XL 500mg, Tab Rithmo XL 500mg	
	» Inj Klaricid 500mg/vial, Inj Rithmo 500mg/vial	
Roxithromycin	» Tab Rulid 100mg, Tab Roxacin 100mg, Tab Pulsate 100mg	
	» Tab Rulid 150mg, Tab Roxacin 150mg	
	» Tab Rulid 300mg, Tab Roxacin 300mg	
Doxycycline	» Cap Vibramycin 100mg, Cap Doxyn 100mg, Cap Wellcodox 100mg	BD
Minocycline	» Tab Minoderm 100mg, Tab Minogen 100mg	BD
Lincomycin	» Cap Lincocin 500mg, Cap Olinc 500mg	BD
	» Inj Lincocin 300mg, Inj Olinc 300mg	
	» Inj Lincocin 600mg, Inj Olinc 600mg	
Clindamycin	» Cap Dalacin-C 150mg	TDS/QID
	» Cap Dalacin-C 300mg	
Gentamicin	» Inj Dalacin-C 600mg/4ml	
	» Inj Gentacin 40mg/1ml, Inj Gentacin 40mg/1ml	
Amikacin	» Inj Gentacin 80mg/2ml, Inj. Gentamicin 80mg/2ml	
	» Inj Gracil 25mg, Inj Amkay 25mg	
	» Inj Gracil 50mg, Inj Amkay 50mg	
	» Inj Gracil 100mg, Inj Amkay 100mg	
	» Inj Gracil 250mg, Inj Amkay 250mg	
Kanamycin	» Inj Gracil 500mg, Inj Amkay 500mg	
	Inj Kanacyn 0.5g/2ml, Inj Kanacyn 1g/4ml	

Tobramycin	Inj. Nebcin 10mg/1ml, 20mg/1ml and 80mg/2ml	
Fosfomycin	» Cap Fosomin 500mg, Cap Focin 500mg, Cap Cynfo 500mg	TDS/QID
	» Inj Focin 1g/vial (Higher doses can be given according infection)	TDS
Vancomycin	» Inj Vancom 1g/vial, Inj Vinjec 1g/vial, Inj Ankotic 1g/vial	TDS/QID
Imipenem + Cilastatin	» Inj Tienam 500mg/vial, Inj Cilapen 500mg/vial, Inj Cilenem 500mg/vial	
Meropenem	» Inj Meronem 500mg/vial, Inj Merpen 500mg/vial, Inj Panro 500mg	
	» Inj Meronem 1g/vial, Inj Merpen 1g/vial, Inj Panro 1g	TDS
Doripenem	» Inj Ronim 500mg/vial, Inj. Dorinem 500mg/vial	
Ertapenem	» Inj Invanz 1g/vial, Inj Ernem 1g/vial	OD
Aztreonam	» Inj Azactam 500mg, Inj Azactam 1g & Inj Azactam 2g	BD/TDS
Fusidic acid	» Tab Fucidin 250mg, Tab Fuciderm 250mg	
Co-trimoxazole	» Tab Septran DS, Tab Nicotrim forte ((160mg/800mg)	BD
Linezolid	» Tab Nezkil 400mg, Tab Barizold 400mg, Tab Ecacil 400mg	
	» Tab Nezkil 600mg, Tab Barizold 600mg, Tab Ecacil 600mg	BD
	» IV infusion 200mg/100ml: Inj Nezkil, Inj Ecasil, Inj Zolrest, Inj Barizold	
	» IV infusion 600mg/300ml: Inj Nezkil, Inj Ecasil, Inj Zolrest, Inj Barizold	
Colistimethate sodium	Inj Colistin 1MIU, 2MIU, 3MIU, 4MIU, 4.5MIU, 5MIU	
	Inj Colomycin 1MIU	
Chloramphenicol	Inj. Chloromycetin	
Streptomycin	Inj. Streptomycin	

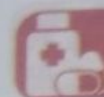
ANTI-DEPRESSANT

GENERIC	BRAND	USUAL DAILY DOSAGE	MAXIMUM DOSE
Fluoxetine	» Cap Prozac 20mg, Cap Flux 20mg » Cap Rize 20mg, Syt Rize 20mg » Cap Depricap 20mg, Syt Depricap 20mg » Cap Floxac 20mg, Tab Floxac 20mg	5-40 Mg	80 Mg
Citalopram	» Tab Cipram 20mg » Tab Celesta 20mg » Tab Cipramil 20mg » Tab Citalo 20mg	20-40 mg	40 mg
Escitalopram	» Tab Cipralex 10mg, 20mg » Tab Estar 5mg, 10mg, 20mg » Tab Pexnew 5mg, 10mg, 20mg » Tab Citanew 5mg, 10mg, 20mg » Drops: Citanew 10mg/ml, Prolexa 10mg/ml	10-20 mg	20 mg
Fluvoxamine	» Tab Flaverin 50mg, 100mg » Tab Voxamine 50mg, 100mg	100-300 mg	300 mg
Paroxetine	» Tab Seroxat 20mg, Tab Seroxate 25mg » Tab Seroxat CR 12.5mg » Tab Paraxyl 20mg » Tab Paraxyl CR 12.5mg, 25mg and 37.5mg	20-30 mg	50 mg



Sertraline	» Tab Zoloft 50mg » Tab Sestrin 50mg and 100mg » Tab Sert 50mg and 100mg » Tab Preloft 50mg and 100mg	50-150 mg	200 mg
Venlafaxine	» Tab Enpress 37.5mg and 75mg » Cap Enpress XR 75mg » Tab Vendep 50mg, Tab Vendep XR 75mg » Cap Effexor XR 75mg and 150mg » Tab Effexor 37.5mg	150-225 mg	225 mg
Desvenlafaxine	» Tab Lafaxine ER 50mg » Tab Depistiq XR 50mg » Tab Venadex ER 50mg	50 mg	100 mg
Duloxetine	» Cap Dulan 20mg, 30mg and 60mg » Cap Lyta 20mg, 30mg and 60mg » Cap Zenbar 20mg, 30mg and 60mg	30-60 mg	120 mg
Imipramine	» Tab Tofranil 25mg » Tab Imidol 25mg	150-300 mg	300 mg
Clomipramine	» Tab Clomfranil 10mg and 25mg	100 mg	250 mg
Amitriptyline	» Tab Tryptanol 25mg » Tab Amyline 25mg » Tab Amitin 25mg	100-300 mg	300 mg
Nortriptyline	» Tab Sensival 25mg	50-150 mg	150 mg
Nortriptyline 10mg+ Fluphenazine 0.5mg	» Tab Motival » Tab Modrine	30-120 mg	150 mg
Mirtazapine	» Tab Remeron 30mg » Tab Mirtazep 15mg and 30mg » Tab Elaxine 15mg and 30mg	15-45 mg	45 mg
Bupropion	» Tab Butrin 75mg » Tab Butrin XL 150mg, and 300mg » Tab Zylexx 75mg » Tab Zylexx SR 150mg and 300mg	30 mg	400 mg
Buspirone	» Tab Busron 5mg » Tab Benzodep 5mg	15-30 mg	60 mg
Trazodone	» Tab Deprel 50mg, 100mg, Deprel drops » Tab Trazolam 50mg » Tab Desryl	100-300 mg	400 mg
Vilazodone	» Viibryd 10mg, 20mg and 40mg	10-40 mg	40 mg
Selegiline	» Tab Selgin 5mg		

Dosulepin	» Tab Prothiaden 25mg, 75mg	25-150 mg	225 mg
Agomelatine	» Tab Agoviz 25mg » Tab Agotine 25mg	25-50 mg	50 mg
Maprotiline	» Tab Ludiomil 10mg, 25mg	100-200 mg	300 mg
Vortioxetine	» Tab. Vrontil 5mg, 10mg and 20mg » Tab. Vorneu 5mg, 10mg and 20mg » Tab. Brintellix 5mg, 10mg and 20mg » Tab. Oxivort 10mg, 20mg	10-20 mg	20 mg



BENZODIAZEPINES/TRUNQUILIZER/ANTI-ANXIETY

Generic	Brand Name	Daily Dosage
Alprazolam	» Tab Xanax 0.25mg, 0.5mg and 1g » Tab Alp 0.25mg, 0.5mg and 1g » Tab Azolam 0.25mg, 0.5mg and 1g	Daily dose: 0.5mg Daily Maximum dose: 4mg
Estazolam	» Tab Esilgan 1mg » Tab Esilgan 2mg	Daily dose: 1mg Daily Maximum dose: 2mg
Midazolam	» Tab Dormicum 7.5mg » Inj Dormicum 5mg/5ml » Inj Idazol 5mg/5ml	
Bromazepam	» Tab Lexotinil 3mg » Tab Relaxin 3mg » Tab Sakoon 3mg » Tab Bromalex 3mg	Daily dose: 3mg to 18mg Daily Maximum dose: 60mg
Lorazepam	» Tab Ativan 1mg, Tab Ativan 2mg » Tab Tenzil 1mg, Tab Tenzil 2mg	Daily dose: 2mg to 4mg Daily Maximum dose: 4mg
Lormetazepam	» Tab Noctamid 1mg	Daily dose: 0.5 to 2mg
Diazepam	» Tab Valium 5mg » Tab Valium 10mg » Inj Valium 10mg/2ml	
Clonazepam	» Tab Revotril 0.5mg, Tab Revotril 2mg » Tab Naze 0.5mg, Tab Naze 2mg » Tab Magura 0.5mg, Tab Magura 2mg » Drops: Revotril, Naze, Epizep	Daily dose: 1mg to 2mg Daily Maximum dose: 60mg
Clorazepate	» Tab Tranxene 5mg and 10mg	Daily dose: 15mg to 30mg Daily Maximum dose: 10mg
Temazepam	» Cap Restoril 15mg, 30mg	Daily dose: 15mg Daily Maximum dose: 30mg
Chlordiazepoxide 5mg	» Tab Librex	Daily dose: 10mg to 20mg Daily Maximum dose: 100mg
Eszopiclone	» Tab Clonexa 1mg, 2mg and 3mg » Tab Eszopic 1mg, 2mg and 3mg	Daily dose: 2mg to 3mg Daily Maximum dose: 3mg
Flunitrazepam	» Tab Rohypnol 2mg	
Nitrazepam	» Tab Mogadon 5mg, 10mg	

Triazolam	» Tab Halcoin 250mcg	Daily dose: 0.125mg Daily Maximum dose: 0.25mg
Etifoxine	» Cap Stresam 50mg	
Zolpidem	» Tab Stilnox 10mg » Tab Zolp 10mg » Tab Xolnox 10mg	Daily dose: 5mg to 10mg Daily Maximum dose: 10mg

ANTI-EPILEPTIC/ANTICONVULSIVE

Generic	Brands	Daily dose	Minimum Number of Daily Doses
Sodium valproate (Valproic acid)	» Tab. Epival 250mg, Tab. Epival 500mg » Tab. Epival CR 500mg » Inj. Epival 500mg/5ml » Tab. Dapakan 250mg, Tab. Dapakan 500mg	1500mg to 2000mg	2-3
Levetiracetam	Tab. Lerace 250mg, Tab. Lerace 500mg Tab. Lumark 250mg, Tab. Lumark 500mg Tab. Epilapsa 250mg, Tab. Epilapsa 500mg Tab. Lerace 500mg XR (Extended Release tablets) Injection 500mg/5ml: Lerace, Lumark, Epilapsa	1000mg to 3000mg	2
Brivaracetam	Tab. Brivatam 25mg, 50mg and 100mg Inj. Brivatam 50mg/5ml Tab. Brivace 25mg, 50mg and 100mg Inj. Brivace 50mg/5ml	50mg to 200mg	2
Carbamazepine	Tab Tegrol 200mg Tab Terol 200mg Tab Seizunil 200mg, 400mg	400 mg to 1600mg	2
Oxcarbazepine	Tab Trioptal 300mg, 600mg Tab Telax 150mg, 300mg, 600mg, Tab Oxalepsy 150mg, 300mg, 600mg	900mg to 1800mg	2
Clorazepate	Tab Tranxene 5mg Tab Tranxene 10mg	22.5mg to 90mg	2
Phenytoin	Cap. Dilantin 30mg, 100mg Tab. Epilantin 100mg Tab. Epitoin 100mg Inj. Epigran 250mg/5ml (Atco)	200mg to 400mg	1
Ethosuximide	Cap. Zarontin 250mg/5ml	500mg to 1500mg	2
Phenobarbitone	Tab Phenobarbitone 30mg Syp Debritone 20mg/5ml	50 - 100mg	2/3
Topiramate	Tab Hitop 25mg, 50mg, and 100mg Tab Topagen 25mg, 50mg, and 100mg Tab Torat 25mg, 50mg, and 100mg	200mg to 400mg	2
Lamotrigine	Tab Lamictol 25mg, 50mg, and 100mg Tab Lomogin 25mg, 50mg, and 100mg Tab Lojin 25mg, 50mg, and 100mg Tab Lamnet 25mg, 50mg, and 100mg	100mg to 500mg	2
Diazepam	Tab. Valium 5mg Tab. Valium 10mg Inj. Valium 10mg/2ml		

Clonazepam	Tab. Revotril 0.5mg and 2mg Tab. Naze 0.5mg and 2mg Tab. Magura 0.5mg and 2mg	0.04mg to 0.2mg/kg	2
Gabapentin	Cap. Neogab 100mg, 300mg, and 400mg Cap. Nervix 100mg, 300mg, and 400mg Cap. Gabix 100mg, 300mg	900mg to 3600mg	3
Pregablin	Cap. Prelin 50mg, 75mg, 100mg, & 150mg Cap. Gabica 50mg, 75mg, 100mg, 150mg, & 300mg Cap. Zeegap 25mg, 50mg, 75mg, 100mg, & 150mg Cap. Syngab 25mg, 50mg, 75mg, 100mg, & 200mg	150mg to 300mg	2
Lacosamide	Tab. Lalap 50mg, 100mg, 150mg and 200mg Inj. Lalap 200mg/20ml Tab. Laclep 50mg, 100mg, and 150mg Inj. Laclep 200mg/20ml (10mg/1ml)	100mg to 400mg	2
Zonisamide	Tab. Zonas 100mg, Tab. Zonegran 100mg	200mg to 600mg	2
Vigabatrin	Tab. Sabril 500mg	3000mg	2
Thiopental	Pentothal sodium 5mg/ampule		

ANTI-PSYCHOTIC

GENERIC	BRAND	USUAL DAILY DOSAGE	MAXIMUM DOSE
Aripiprazole	Tab. Aripip 10mg, 15mg Tab. Adablizer 10mg, 15mg Tab. Profy 10mg, 15mg	10-15mg	30mg
Chlorpromazine	Tab. Largactil 25mg, 100mg	100-400mg	1g
Clozapine	Tab. Clozaril 100mg Tab. Amlepo 100mg Tab. Saveril 100mg	300-450mg	900mg
Fluphenazine	Inj. Flucate 25mg/1ml Inj. Modecate 25mg/1ml Inj. Psycate 25mg/1ml	2-10mg	60mg
Fluphenazine with Nortriptyline)	Tab. Modrin Tab. Motival		
Haloperidol	Tab. Serenace 1.5mg, 5mg, 10mg Inj. Serenace 5mg/1ml Tab. Dosik 1.5mg, 5mg, 10mg Syp. Dosik 2mg/ml	2-5mg	60mg
Illoperidone	Tab. Ilodon 2mg, 4mg, 6mg, 12mg	12-24mg	24mg
Lurasidone	Tab. Lurisa 40mg, 80mg	40-80mg	80mg
Olanzapine	Cap. Olanzia 5mg, 10mg Tab. Olepra 5mg, 10mg Tab. Nirvanol 5mg, 10mg	5-10mg	20mg
Paliperidone	Tab. Paliris XR 1.5mg, 3mg Tab. Vegadon 3mg, 6mg	6-12mg	12mg
Prochlorperazine	Tab. Stemetil 5mg		
Quetiapine	Tab. Qusel 25mg, 100mg, 200mg, 300mg Tab. Qutyl 25mg, 100mg, 200mg, 300mg Tab. Evokalm 25mg, 100mg Tab. Seroquel 25mg, 100mg Tab. Risperdal 1mg, 2mg, 3mg and 4mg Syp. Risperdal 1mg/5ml	200-400mg	800mg

Risperidone	Tab. Risp 1mg, 2mg, 3mg and 4mg Syp. Risp 1mg/5ml Tab. Espidone 1mg, 2mg, 3mg and 4mg Syp. Espidone 1mg/5ml Tab. Isrip 1mg, 2mg, 3mg and 4mg Tab. Buzon 1mg, 2mg, 3mg and 4mg	2-6mg	10mg
Trifluoperazine	Tab. Stelazine 1mg, 5mg Tab. Estezene 1mg, 5mg	5-15mg	60mg
Ziprasidone	Cap. Zeldox 40mg, 60mg Cap. Xepex 20mg, 40mg Cap. Ziprawin 20mg, 40mg	40-160mg	160mg
Zuclopenthixol	Tab. Clopixol 2mg, 10mg, and 25mg Inj. Clopixol Acuphase 50mg/1ml Inj. Clopixol Acuphase 100mg/2ml Inj. Clopixol Depot 200mg/1ml	The recommended dose range is 15 to 50 mg/day to the maximum licensed dose of 600 mg weekly.	

ANTI-ALLERGIC/ANTIHISTAMINE

Pheniramine maleate	» Tab Avil 25mg (Sanofi Aventis) » Syp Avil 15mg/5ml » Inj Avil 50mg/2ml
Hydroxyzine	» Tab Atarax 10mg » Tab Atarax 25mg
Clemastine	» Tab Tandegyl 1mg, Tab Tandegyl 2mg » Tab Klemat 1mg, Tab Klemat 2mg
Ketotifen	» Syp Zatofen 1mg/5ml, Tab Zatofen 1mg » Syp Asthotifen 1mg/5ml, Tab Asthotifen 1mg » Syp Aria 1mg/5ml, Tab Aria 1mg » Syp Mactifen 1mg/5ml, Cap Mactifen 1mg
Cetirizine	» Tab Rigix 10mg, Syp Rigix 5mg/5ml, Rigix Drops 10mg/ml » Tab Zyrtec 10mg, Syp Zyrtec 5mg/5ml » Tab Baydal 10mg, Syp Baydal 5mg/5ml
Levocetirizine	» Tab Belair 5mg, Tab Xyzal 5mg, Tab Leozin 5mg » Tab T-day 5mg, Syp T-day 2.5mg/5ml » Tab Neo-Sedil 5mg, Syp Neo-Sedil 2.5mg/5ml
Ebastine	» Tab Kestine 10mg, 20mg » Syp Kestine 5mg/5ml » Tab. Ebaget-D 10mg and 20mg » Tab Beceptor 10mg, 20mg
Loratidine	» Tab Lorin NSA 10mg, Syp Lorin NSA 5mg/5ml » Tab Softin 10mg, Syp Softin 5mg/5ml » Tab Loril 10mg, Syp Loril 5mg/5ml » Tab Xylor 10mg, Syp Xylor 5mg/5ml
Loratidine 5mg, Pseudoephedrine 60mg	» Tab. Rhilor-D
Desloratadine	» Tab Destina 5mg, Tab Larinex 5mg » Tab Neo-Antial 5mg, Syp Neo-Antial 0.5mg/ml » Tab Jordin-D 5mg, Syp Jordin-D 0.5mg/ml
Fexofenadine	» Tab Telfast 60mg, 120mg, 180mg » Tab Fexet 60mg, 120mg, 180mg » Tab Fexo 60mg, 120mg, 180mg » Tab Xadin 60mg, 120mg, 180mg
Fexofenadine 60mg + Pseudoephedrine 120mg	» Tab Telfast-D » Tab Fexet-D » Tab Fexo-D » Tab Xadin Plus (Fexo 60mg+ Pseudoephedrine 60mg)

ANTI-EMETIC/ANTI-VERTIGO

Promethazine	» Syp Phenergan » Tab Avomine 25mg
Dimenhydrinate	» Tab Gravinate 50mg » Syp Gravinate 12.5mg/5mg » Inj Gravinate 50mg/1ml
Doxylamine 10mg + Pyridoxine (Vitamin-B6) 10mg	» Tab Envepe » Tab Xyquil DR » Tab Femiroz
Cyclizine	» Tab Marzine 50mg » Syp Marzine 12.5mg/ml » Inj Marzine 50mg
Meclozine (Meclizine) + Pyridoxine (Vitamin-B6)	» Tab Navidoxine
Cinnarizine	» Tab Stugeron 25mg » Cap Stugeron 75mg
Domperidone + Cinnarizine	» Tab Pelton-C » Syp Pelton-C
Chlorpromazine	» Tab Largactil 10mg, 25mg
Prochlorperazine	» Tab Stemetil 5mg
Metoclopramide	» Tab Maxolon, Syp Maxolon, Inj Maxolon » Tab Metaclon, Syp Metaclon, Inj Metaclon
Domperidone	» Tab Motilium 10mg, Syp Motilium » Tab Domel 10mg, Syp Domel » Tab Vomilux 10mg, Syp Vomilux
Ondansetron	» Tab Zofran 8mg, Inj Zofran 4mg/2ml, Inj Zofran 8mg/4ml » Tab Onset 8mg, Inj Onset 8mg/4ml » Tab Onseron 8mg, Inj Onseron 4mg/2ml, Syp Onseron 4mg
Granisteron	» Tab Graniset 1mg
Aprepitant	» Cap. Apreon 80mg » Cap. Apreon 125mg
Betahistine	» Tab Serc 8mg, Tab Serc 16mg, Tab Serc 24mg » Tab Enier 8mg, Tab Enier 16mg, Tab Enier 24mg » Tab Dowbet 8mg, Dowbet 16mg, Dowbet 24mg » Tab Setspin 8mg, Setspin 16mg, Setspin 24mg



ANTI-PEPTIC ULCER/GERD DRUG BRAND IN PAKISTAN

Famotidine	» Tab Reducid 20mg, Tab Reducid 40mg, Syb Reducid 10mg » Tab Polypep 20mg, Tab Polypep 40mg, Syb Polypep 10mg » Tab Acicon 20mg, Tab Acicon 40mg, Syb Acicon 10mg » Tab Famopsin 20mg, Tab Famopsin 40mg » Tab Famot 20mg, Tab Famot 40mg, Syb Famot 10mg » Inj Famot 40mg/4ml x IV (diluted in 100ml 0.9% N/S)
Cimetidine	» Tab Tagamet 200mg, Tab Tagamet 400mg » Tab Cimet 400mg, Syb Cimet 100mg » Tab Ulcerex 400mg, Syb Ulcerex 100mg » Injection = 200mg/2ml: Inj Ulcerex, Inj Cimetamat x IM/IV Infusion
Omeprazole	» Cap Ruling 20mg (BD), Cap Ruling 40mg (OD) » Cap Omezol 20mg (BD), Cap Omezol 40mg (OD) » Cap Zoltar 20mg (BD), Cap Zoltar 40mg (OD) » Cap Risek 20mg (BD), Cap Risek 40mg (OD) » Cap Sante 20mg (BD), Cap Sante 40mg (OD) » Injection Brand: Inj Ruling 40mg/vial, Inj Omezol 40mg/vial, Inj Zoltar 40mg/vial, Inj Ruling 40mg/vial, Inj Sante 40mg/vial
Omeprazole + Sodium bicarbonate	» Cap Mep-B 20/1100mg, Cap Mep-B 40/1100mg » Cap Faast plus 20/1100mg, Cap Faast plus 40/1100mg » Cap Teph Insta 20/1100mg, Cap Teph Insta 40/1100mg » Sachets powder form (soluble in a glass water): » Teph insta 20/1680mg sachet x (BD) » Teph insta 40/1680mg sachet x (OD) » Risek insta 20/1680mg sachet x (BD) » Risek insta 40/1680mg sachet x (OD)
Esomeprazole	» Cap Esso 20mg (BD), Cap Esso 40mg (OD) » Cap Nexum 20mg (BD), Cap Nexum 40mg (OD) » Cap Esomax 20mg (BD), Cap Esomax 40mg (OD) » Cap NovoTEpH 20mg (BD), Cap NovoTEpH 40mg (OD) » Cap Esante 20mg (BD), Cap Esante 40mg (OD) » Injection Brand: Inj Esso 40mg/vial, Inj Nexum 40mg/vial, Inj Esomax 40mg/vial, Inj NovoTEpH 40mg/vial, Inj Esante 40mg/vial
Pantoprazole	» Tab Zopent 20mg (BD), Tab Zopent 40mg (OD) » Tab Zentro 20mg (BD), Tab Zentro 40mg (OD) » Tab Neege 20mg (BD), Tab Neege 40mg (OD) » Injection Brand: Inj Zopent 40mg/vial, Inj Zentro 40mg/vial, Inj Neege 40mg/vial
Lansoprazole	» Cap Qpro 15mg (BD), Cap Qpro 30mg (OD) » Cap Lanzol 30mg, Cap Lanzit 30mg, Tab SElanzSR 30mg » Injection = 30mg/vial: Inj Qpro, Inj SElanzSR, (diluted in 100ml N/S)
Rabeprazole	» Tab Repar 10mg, Tab Repar 20mg » Tab Rabosh 10mg, Tab Rabosh 20mg » Tab Rabecid 10mg, Tab Rabecid 20mg » Tab Novipraz 10mg, Tab Novipraz 20mg
Dexlansoprazole	» Cap Dolgina 30mg, Cap Dolgina 60mg » Cap Razodex 30mg, Cap Razodex 60mg » Cap Dextop 30mg, Cap Dextop 60mg
Vonoprazan	» Tab. Vocinti 10mg (BD), Tab Vocinti 20mg (OD) » Tab Voniza 10mg (BD), Tab Voniza 20mg (OD)

Sucralfate	» Tab Vonozan 10mg (BD), Tab Vonozan 20mg (OD)
	» Tab Vonnp 10mg (BD), Tab Vonnp 20mg (OD)
	» Tab Ulsanic 500mg, Tab Ulsanic 1g
	» Syp Ulsanic 1g/5ml
	» Syp Surlka 1g/5ml
Sucralfate + Calcium carbonate	» Syp Crafilm 1g/5ml
	» Tab Crafilm 250mg (chewable)
Bismuth subsalicylate	» Syp Bismol 88mg/5ml
	» Tab Bismol 265mg
Levosulpiride	» Tab Levopraid 25mg, Tab Levopraid 50mg
	» Tab Sulvorid 25mg, Tab Sulvorid 50mg
	» Tab Pride 25mg, Tab Pride 50mg
	» Tab Dowsul 25mg, Tab Dowsul 50mg
	» Tab Scipride 25mg, Tab Scipride 50mg
Itopride	» Tab Ganaton 50mg, Tab Ganaton 150mg (OD)
	» Tab ITP 50mg, Tab ITP 150mg (OD)
	» Tab Noger 50mg, Tab Noger 150mg (OD)
	» Tab Tespral 50mg, Tab Tespral 150mg (OD)
	» Tab Itoguard 50mg, Tab Itoguard 150mg (OD)
Cinitapride	» Tab Cinita 1mg
	» Tab Cidine 1mg
	» Tab Cinirant 1mg



ANACID/ANTIPLATULANTS/ANTISPASMODIC

COMPOSITION	BRAND
Magnesium Oxide, Aluminium Hydroxide, Simethicone & Dicyclomine HCl	» Syp Colenticon Gel
Oxethazaine, Magnesium Oxides and Hydroxides, Aluminium Hydroxide and Oxide	» Syp Mucain
Aluminum Hydroxide, Magnesium Hydroxide, Simethicone	» Syp Manacid (Sugar free)
+Extra strength	» Syp Manacid forte (Sugar free)
Sodium Alginate, Sodium Bicarbonate, Calcium Carbonate	» Syp Gaviscon
+Extra strength with Potassium Bicarbonate	» Syp Gaviscon advance
Sodium Alginate, Potassium Bicarbonate	» Syp Lagita advance (Sugar free)
Aluminum Hydroxide, Magnesium Hydroxide, Simethicone	» Syp Dijex MP
	» Syp Mylanta-2
	» Syp Amrocon
Calcium Carbonate and Sodium Bicarbonate, Fennel & Mint	» Syp Digas
	» Digas drops (children's)
	» Colorest drops (Children's)
Herbal: Fennel, Chamomile, Mint Dry Extract	» Syp Hilgas (Sugar free)
Herbal extracts with dietary fiber wheat dextrin	» Syp Koolox
Aluminum phosphate, Simethicone	» Tab Nospa 40mg
	» Tab Nospa forte 80mg
	» Tab Relispa 40mg
	» Tab Relispa forte 80mg
	» Inj Nospa 40mg/2ml
	» Inj Relispa 80mg/4ml
Drotaverine	» Tab Colofac 135mg
	» Tab Zeespa 135mg
Mebeverine	» Tab Spasler Neo 135mg

	» Cap Despas MR 200mg » Cap Mebever MR 200mg
Hyoscine	» Tab Buscopan Plus » Syp Spasler-P » Tab Anapas 80mg » Anapas drops
Phloroglucinol + Trimethylphloroglucinol	» Tab Spasfon, Inj Spasfon » Tab SpasRid, Inj. SpasRid » Tab Anafortan plus, Inj Anafortan plus



COMMONLY USED LAXATIVE (CONSTIPATION) DRUG BRAND IN PAKISTAN

Lactulose	» Syp Lilac » Syp Duphalac
Sodium picosulphate	» Syp Laxoberon » Tab Laxoberon » Tab. Conspic » Conspic drops » Tab. Skilex » Skilax drops
Becacodyl	» Tab Delax » Tab Dulcolex

MUSCLE RELAXANT

Tizanidine	» Tab Ternelin 2mg OR 4mg » Tab Movax 2mg OR 4mg » Tab Musidin 2mg, 4mg, Cap Musidin 6mg
Cyclobenzaprine	» Tab Eumytic 5mg, Tab Eumytic 5mg » Tab Emrix SR 15mg, Tab Emrix SR 30mg » Tab Mezrel XR 15mg, Tab Mezrel XR 30mg
Baclofen	» Tab Lioresal 10mg » Tab Flexibil 10mg » Tab Baclin 10mg
Eperisone	» Tab Myonal 50mg
Thiocolchicoside	» Cap Muscoril 4mg, Inj Muscoril 4mg/2ml (I/M) » Cap Thiolax 4mg, Inj Thiolax 4mg/2ml (I/M) » Cap Muscolin 4mg, Inj Muscolin 4mg/2ml (I/M)
Paracetamol + Orphenadrine	» Tab Neubrol, Tab Neubrol forte » Tab Sinaxamol, Tab Sinaxamol plus » Tab Duragesic, Tab Duragesic forte
Acetaminophen + Methocarbamol	» Tab Bexamin
Diazepam	» Tab Valium 5mg, 10mg » Inj Valium 10mg/2ml

MULTIVITAMINS/IRON & SUPPLEMENTATION

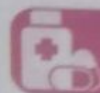
FORMULA	BRAND
Vitamin-C, E, B1, B2, B6, B12, Nicotinamide, Calcium pantothenate, Folic Acid	» Tab Becefol
Vitamin B2, B1, Ascorbic Acid, Calcium Pantothenate, Cyanocobalamin, Pyridoxine	» Tab Surbex-T
Nicotinamide, D-Pantothenol, Vitamin B2, Vitamin B1, Ascorbic Acid, Calcium Pantothenate, Cyanocobalamin, Pyridoxine	» Syp Surbex
Nicotinamide, Riboflavin, Thiamine HCl (Vitamin B1), Cyanocobalamin	» Syp Polybion forte » Cap Polybion-Z
Ferrous sulphate (represent elemental iron), Folic Acid, Vitamin-C, B1, B2, B6, B12, Nicotinamide, Calcium, pantothenate	» Syp Iberet 500 » Tab Iberet folic 500
Ferrous sulphate (represent elemental iron), Folic Acid, B-Complex	» Cap. Fefolvit » Cap Fefol
A to Z	» Tab Centrum » Tab Surbex-Z » Tab Vitrum » Tab Revital-Multi
Multivitamins	» Tab Optilets-M » Tab Dayalets
Iron + B-Complex	» Cap. Singobion » Syp. Singobion
Iron + Vitamins with Folic acid	» Cap Fefolvit
Vitamin B-Complex + Vitamin-C + Lysine	» Syp Lysovit
Vitamin B-Complex	» Syp Leaderplex
Vitamin B-Complex + Iron + Lysine	» Syp Incremin
Vitamin A,D,C B-Complex and Nicotinamide	» Syp Vidaylin
Vitamin A,D,C, B-Complex, Nicotinamide, Panthenol, Iron, Iodine, Calcium, Phosphorus, Manganese, Magnesium, Zinc, Choline and Inositol	» Syp Vidaylin-M
Vitamin A,E,C,D B-Complex, Nicotinic Acid, Cyanocobalamin, Folic Acid, Pyridoxine and Lysine	» Syp Vidaylin-L
Vitamin A,D,C B-Complex and Nicotinamide	» Vidaylin drop
Vitamin A, Vitamin B1, Vitamin B12, Vitamin B2, Vitamin B6, Vitamin C, Vitamin D, Choline, Inositol, Lysine, Nicotinamide	» Tab Vidaylin-T » Tab Cecon » Cecon drop » Tab Chewcal
Vitamin-C	» Tab. Neurobion » Inj. Neurobion
Vitamin-B1, B6, B12 (Thiamine, Pyridoxine, Cyanocobalamin)	



	» Tab. Neuro-Bedoxine » Inj. Neuro-Bedoxine » Tab Bevidox
Vitamin-A, D, E, C, B1, B2, B12, Nicotinamide, Magnesium Carbonate, Folic Acid, Iron, Calcium Pantothenate, Pyridoxine and Copper	» Tab Theragran-H
Potassium, Vitamin-A, D, E, C, B1, B2, B12, Selenium, Zinc, Chloride, Biotin, Calcium Carbonate, Folic Acid, Iron, Iodine, Magnesium and Pantothenic Acid	» Tab Theragran-M
Vitamin-A (B-Carotene), D, E, C, B1, B2, B6, B12, Pantothenic Acid, Biotin, Folic acid, Niacin, Iron, Calcium, phosphorus, iodine, Magnesium, copper, zinc, manganese, Selenium, molybdenum, chromium, potassium, chloride	» Tab Theragran Ultra
Calcium, vitamin C ± other vitamins	» Tab Abocal » Tab CAC 1000 plus » Tab Berocca » Tab Redoxone
Vitamin-D3 600'000 IU (6 Lac IU) x IM	» Inj Vitamin-D3
Syp Calcium Phosphate 210mg + Vitamin-D 350 unit	» Tab Calcium-P
Tab Calcium Phosphate 400mg + Vitamin-D 5mcg (200 IU)	» Syp Calcium-P
Calcium Carbonate, Vitamin D3	» Tab Caldree-600mg
Calcium, Vitamin D, Minerals	» Tab Calcite 600mg
Vitamin D3, Calcium, magnesium, zinc	» Tab Ostebon plus » Tab Osteocare » Syp Osteocare » Tab. Avelia
Cholecalciferol (Vitamin D3)	» Cap. Opt-D 25000IU, Cap. Opt-D 100000IU, Cap. Opt-D 200000IU » Cap. Dan-D 5000IU, Cap. Dan-D 50000IU, Cap. Dan-D 100000IU, Cap. Dan-D 200000IU » Drops: Opt-D 400IU, Miura-D 400IU, and All-D 400IU » Injections: inj. Indrop-D, inj. D-All Inj.D-Tres and Inj. Miura-D
Vitamin-E	» Cap Evion 200mg » Cap. Evion 400mg » Cap. Evion 600mg
A to Z supplement for hairs, nails and skin (hairs loss and growth)	» Tab Perfactil Original » Tab Hairvit » Tab. Hairlife » Tab. Dermazon
High Potency hematinic compounds	» Tab Trihemic 600
Vitamin-A, D, E, C, B1, B2, B12, Folic Acid, Calcium pantothenate, Calcium, Iodine, Elemental Iron and Copper.	» Tab Pramit FA
Tab Folic acid 5mg	» Tab Folic acid
L-Methylefolate	» Tab Myfol 400mg » Syp Myfol 400mcg » Myfol drops



	» Tab Maxfol 400mcg » Tab Folat 400mcg » Tab Adfolic 300mcg and 600mcg
Mecobalamin 500mcg	» Tab. Methycobal » Inj. Methycobal » Tab. Neuromet » Inj. Neuromet » Tab. Cobalmin » Inj. Cobalmin » Tab. Incobal » Inj. Incobal
L-Methylefolate, Pyridoxal phosphate, Methycobalamin	» Tab. Nervita » Tab. Metaner
Omega-3 Fish Oil Plus Cod Liver Oil	» Seven seas Softgel
Iron Polymaltose	» Syp. Maltofer » Tab. Maltofer » Syp. Malcifer » Tab. Malcifer » Syp. Ferosoft » Tab. Ferosoft » Ferosoft drops
Iron Polymaltose + Folic acid	» Syp. Maltofer Fol » Tab. Maltofer Fol » Tab. Malcifer-F » Syp. Malcifer-F
Iron sucrose 100mg/5ml	» Inj Venofer » Inj Besleri-S » Inj Irose
Iron sucrose complex	» Inj. Ferosoft-S 5ml/ampule
Iron carboxymaltose 500mg/10ml	» Inj Fercari 500mg/10ml » Inj. FCM 500mg/10ml » Inj. Ferinject 500mg/10ml
Multivitamins	» Inj Multibionta 10ml/ampule
Multivitamins	» Inj Bejectal-T
Iron isomaltoside 1000 100mg/1ml	» Inj Monofer



ANTI-VIRAL

Ribavirin	Cap Ribazole 400mg, & Tab Ribazole 500mg, 600mg Cap Ribavil 400mg, 500mg and 600mg
Aciclovir	Tab Zovirax 200mg, Zovirox 5% w/w 10g cream Zovirax ophthalmic ointment 4.5g Tab Acylex 200mg, 400mg and 800mg Acylex 5% w/w cream, Syp Acylex 200mg/60ml Tab Cycloz 200mg, 400mg and 800mg Syp Cycloz 200mg/60ml, Cycloz 5% cream Inj Cycloz 250mg/vial (Highnoon) Inj Acyclovir 500mg/10ml vial (ABBOTT) Inj Aclovir 250mg/10ml vial, and 500mg/10ml vial (Genix)
Famciclovir	Tab Viracure 250mg (Atco), Tab Famvir 250mg (Novartis)
Sofosbuvir	Tab Sofiget 400mg, Tab Sofohil 400mg, Tab Sofomac 400mg
Daclatasvir	Tab Clavir 60mg, Tab Daclaget 60mg, Tab Dacrive
Tenofovir disoproxil fumarate	Tab Tenofo-B 300mg
Tenofovir Alafenamide	Tab Tenofoamide 25mg
Entecavir	Tab Ecavir 0.5mg, Tab Tacavir 0.5mg, Tab Centaurus 0.5mg
Sofosbuvir 400mg + Velpatasvir 100mg	Tab Velpaget, Tab Hilvel
Ledipasvir 90mg + Sofosbuvir 400mg	Tab Syneget-LS, Tab Sofopas
Oseltamivir	Cap Tamflu 75mg
Favipiravir	Tab. Piravir 200mg Tab. Favuza 200mg
Remdesivir	Inj. Mdestiv 100mg/vial Inj. Remidia 100mg/vial Inj. Bemsivir 100mg/vial Inj. Revona 100mg/vial
Methisoprinol	Tab. Isoprinosine 500mg Syp. Isoprinosine 250mg/5ml